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(21) International Application Number: PCT/US00/02200 (22) International Filing Date: 27 January 2000 (27.01.00) (30) Priority Data: 60/117,405 27 January 1999 (27.01.99) US (71) Applicant: ELITRA PHARMACEUTICALS, INC. [US/US]; Suite A, 3510 Dunhill Street, San Diego, CA 92121 (US). (72) Inventors: ZYSKIND, Judith; 8514 La Jolla Scenic Drive, La Jolla, CA 92047 (US). OHLSEN, Kari, L.; 3560 Vista De La Orilla, San Diego, CA 92117 (US). TRAWICK, John; 7210 Baldrich Street, La Mesa, CA 91942 (US). FORSYTH, R., Allyn; 1135 Beryl Street, San Diego, CA 92109 (US). FROELICH, Jamie, M.; 5057 35th Street, San Diego, CA 92116 (US). CARR, Grant, J.; 2210 Sunrise Glen, Escondido, CA 92029 (US). YAMAMOTO, Robert, T.; 3725 Norte Dame Avenue, San Diego, CA 92131 (US). XU, H., Howard; 11142 Ivy Hill Drive, San Diego, CA 92131 (US). (74) Agent: REISMAN, Joseph, M.; Knobbe, Martens, Olson & Bear, LLP, 16th Floor, 620 Newport Center Drive, Newport Beach, CA 92660 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>	
(54) Title: GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN <i>ESCHERICHIA COLI</i>			
(57) Abstract <p>The sequences of nucleic acids encoding proteins required for <i>E. coli</i> proliferation are disclosed. The nucleic acids can be used to express proteins or portions thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous genes that are required for proliferation in microorganisms other than <i>E. coli</i>. The nucleic acids can also be used to design expression vectors and secretion vectors. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms as well as to screen for antimicrobial agents.</p>			

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**GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN
*ESCHERICHIA COLI***

BACKGROUND OF THE INVENTION

Since the discovery of penicillin, the use of antibiotics to treat the ravages of bacterial infections has saved millions of lives. With the advent of these "miracle drugs," for a time it was popularly believed that humanity might, once and for all, be saved from the scourge of bacterial infections. In fact, during the 1980s and early 1990s, many large pharmaceutical companies cut back or eliminated antibiotics research and development. They believed that infectious disease caused by bacteria finally had been conquered and that markets for new drugs were limited. Unfortunately, this belief was overly optimistic.

The tide is beginning to turn in favor of the bacteria as reports of drug resistant bacteria become more frequent. The United States Centers for Disease Control announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of the common *Staphylococcus aureus* (staph). This organism is commonly found in our environment and is responsible for many nosocomial infections. The import of this announcement becomes clear when one considers that vancomycin was used for years to treat infections caused by stubborn strains of bacteria, like staph. In short, the bacteria are becoming resistant to our most powerful antibiotics. If this trend continues, it is conceivable that we will return to a time when what are presently considered minor bacterial infections are fatal diseases.

There are a number of causes for the predicament in which practitioners of medical arts find themselves. Over-prescription and improper prescription habits by some physicians have caused an indiscriminate increase in the availability of antibiotics to the public. The patient is also partly responsible, for even in instances where an antibiotic is the appropriate treatment, patients will often improperly use the drug, the result being yet another population of bacteria that is resistant, in whole or in part, to traditional antibiotics.

The bacterial scourges that have haunted humanity remain, in spite of the development of modern scientific practices to deal with the diseases that they cause. Drug resistant bacteria are now advancing on the health of humanity. A new generation of antibiotics to once again deal with the pending health threat that bacteria present is required.

Discovery of New Antibiotics

As more and more bacterial strains become resistant to the panel of available antibiotics, new compounds are required. In the past, practitioners of pharmacology would have to rely upon traditional methods of drug discovery to generate novel, safe and efficacious compounds for the treatment of disease. Traditional drug discovery methods involve blindly testing potential drug candidate-molecules, often selected at random, in the hope that one might prove to be an effective treatment for some disease. The process is painstaking and laborious, with no guarantee of success. Today, the average cost to discover and develop a new drug is nearly US \$500 million, and the average time is 15 years from laboratory to patient. Improving this process, even incrementally, would represent a huge advance in the generation of novel antimicrobial agents.

Newly emerging practices in drug discovery utilize a number of biochemical techniques to provide for directed approaches to creating new drugs, rather than discovering them at random. For example, gene sequences and proteins encoded thereby that are required for the proliferation of an organism make for excellent targets since exposure of bacteria to compounds active against these targets would result in the inactivation of the organism. Once a target is identified, biochemical analysis of that target can be used to discover or to design molecules that interact with and alter the functions of the target. Using physical and computational techniques, to analyze structural and biochemical targets in order to derive compounds that interact with a target is called rational drug design and offers great future potential. Thus, emerging drug discovery practices use molecular modeling techniques, combinatorial chemistry approaches, and other means to produce and screen and/or design large numbers of candidate compounds.

Nevertheless, while this approach to drug discovery is clearly the way of the future, problems remain. For example, the initial step of identifying molecular targets for investigation can be an extremely time consuming task. It may also be difficult to design molecules that interact with the target by using computer modeling techniques. Furthermore, in cases where the function of the target is not known or is poorly understood, it may be difficult to design assays to detect molecules that interact with and alter the functions of the target. To improve the rate of novel drug discovery and development, methods of identifying important molecular targets in pathogenic microorganisms and methods for identifying molecules that interact with and alter the functions of such molecular targets are urgently required.

Escherichia coli represents an excellent model system to understand bacterial biochemistry and physiology. The estimated 4288 genes scattered along the 4.6×10^9 base pairs of the *Escherichia coli* (*E. coli*) chromosome offer tremendous promise for the understanding of bacterial biochemical processes. In turn, this knowledge will assist in the development of new tools for the diagnosis and treatment of bacteria-caused human disease. The entire *E. coli* genome has been sequenced, and this body of information holds a tremendous potential for application to the discovery and development of new antibiotic compounds. Yet, in spite of this accomplishment, the general functions or roles of many of these genes are still unknown. For example, the total number of proliferation-required genes contained within the *E. coli* genome is unknown, but has been variously estimated at around 200 to 700 (Armstrong, K.A. and Fan, D.P. Essential Genes in the *metB-malB* Region of *Escherichia coli* K12, 1975, J. Bacteriol. 126: 48-55).

Novel, safe and effective antimicrobial compounds are needed in view of the rapid rise of antibiotic resistant microorganisms. However, prior to this invention, the characterization of even a single bacterial gene was a painstaking process, requiring years of effort. Accordingly, there is an urgent need for more novel methods to identify and characterize bacterial genomic sequences that encode gene products required for proliferation and for methods to identify molecules that interact with and alter the functions of such genes and gene products.

SUMMARY OF THE INVENTION

One embodiment of the present invention is a purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 1-81, 405-485, wherein said nucleic acid inhibits microorganism proliferation. The nucleic acid sequence may be complementary to at least a portion of a coding sequence of a gene whose expression is required for

microorganism proliferation. The nucleic acid sequence may comprise a fragment of one of SEQ ID NOs. 1-81, 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The nucleic acid sequence may be complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1-81, 405-485. The promoter may be active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a host cell containing the vectors described above.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242. One aspect of this embodiment is a fragment of the nucleic acid comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

Another embodiment of the present invention is a vector comprising a promoter operably linked to the nucleic acids of the preceding embodiment.

Another aspect of the present invention is a purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters. The nucleic acid may be from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a host cell containing the vector of the preceding embodiment.

Another embodiment of the present invention is purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is an antibody capable of specifically binding the polypeptide of the preceding embodiment.

Another embodiment of the present invention is method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell. The method may further comprise the step of isolating said protein.

Another embodiment of the present invention is a method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

Another embodiment of the present invention is method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide comprising a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

The activity may be an enzymatic activity. The activity may be a carbon compound catabolism activity. The activity may be a biosynthetic activity. The activity may be a transporter activity. The activity may be a transcriptional activity. The activity may be a DNA replication activity. The activity may be a cell division activity.

Another embodiment of the present invention is a compound identified using the above method.

Another embodiment of the present invention is method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

contacting said target with a candidate compound; and
measuring an activity of said target.

The target may be a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA. The target may be a coding region of one of SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may, further comprise the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level. The sub-lethal concentration of said inducer may be such that growth inhibition is 8% or more. The inducer may be isopropyl-1-thio- β -D-galactoside. The growth inhibition may be measured by monitoring optical density of a culture growth solution. The gene product may be a polypeptide. The gene product may be an RNA. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene. The compound may be an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof. The proliferation inhibiting portion of one of SEQ ID NOs. 1-81, 405-485

may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The compound may be a triple helix oligonucleotide.

Another embodiment of the present invention is a preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier. The proliferation-inhibiting portion of one of SEQ ID NOs. 1-81, 405-485 may comprise at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485.

Another embodiment of the present invention is a method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene. The antisense nucleic acid may be complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242. The antisense nucleic acid may be a sequence of one of SEQ ID NOs.: 1-81, 405-485, or a portion thereof. The cell may be contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide. The cell may be contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell. The cell may be contacted with said antisense nucleic acid by electroporation. The antisense nucleic acid may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242. The antisense nucleic acid may be an oligonucleotide.

Another embodiment of the present invention is a method for identifying bacterial strains comprising the steps of:

providing a sample containing a bacterial species; and

identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 1-81, 405-485, 82-88, 90-242.

Another embodiment of the present invention is a method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

- (c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and
- (d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

- (a) identifying a gene or gene product required for proliferation in a first microorganism;
- (b) identifying a homolog of said gene or gene product in a second microorganism;
- (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;
- (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (e) contacting the sensitized microorganism of step (d) with a compound; and
- (f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

The step of identifying a gene involved in proliferation in a first microorganism may comprise:

introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters. The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene. The step of identifying a homolog of said gene in a second microorganism may comprise expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism. The inhibitory nucleic acid may be an antisense nucleic acid. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of said homolog. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding said homolog. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise directly contacting said second microorganism with said nucleic acid. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise expressing an antisense nucleic acid to said homolog in said second microorganism.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method of assaying a compound for the ability to inhibit proliferation comprising:

- (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
- (b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and
- (d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

The inhibitory nucleic acid may be an antisense nucleic acid which inhibits the proliferation of said first microorganism. The inhibitory nucleic acid may comprise a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism. The inhibitory nucleic acid may comprise an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for assaying compounds for activity against a biological pathway required for proliferation comprising:

- sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;
- contacting the sensitized cell with a compound; and
- determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may further comprise contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level. The sublethal level of said antisense nucleic acid

may inhibit proliferation by 8% or more. The agent may be isopropyl-1-thio- β -D-galactoside (IPTG). The inhibition of proliferation may be measured by monitoring the optical density of a liquid culture. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is a compound identified using the method above.

5 Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit cellular proliferation comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and

10 determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antisense nucleic acid to a gene or operon required for proliferation. The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antibiotic. The cell may contain a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell. The antisense nucleic acid may be directed against the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed. The antisense nucleic acid may be directed against a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

20 Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

25 contacting said cell with an antibiotic, wherein the a biological pathway on which said antibiotic acts is known; and

determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

30 Another embodiment of the present invention is a method for determining the pathway on which a test compound acts comprising:

(a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

35 (c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

The method may further comprise:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

Another embodiment of the present invention is a purified or isolated nucleic acid comprising a sequence selected from the group consisting of 1-81, 405-485, 82-88, 90-242, 358, 399-402.

Another embodiment of the present invention is a compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

Another embodiment of the present invention compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

Another embodiment of the present invention is a compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an IPTG dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing either an antisense clone to the *E. coli* ribosomal protein rplW (AS-rplW) which is required for protein synthesis and essential cell proliferation, or an antisense clone to the *elaD* (AS-*elaD*) gene which is not known to be involved in protein synthesis and which is also essential for proliferation.

Figure 2A is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to rplW(AS-rplW) in the presence of 0, 20 or 50 μ M IPTG.

Figure 2B is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to *elaD* (AS-*elaD*) in the presence of 0, 20 or 50 μ M IPTG.

Figure 3 is a graph showing the fold increase in tetracycline sensitivity of *E. coli* transfected with antisense clones to essential ribosomal proteins L23 (AS-rplW) and L7/L12 and L10 (AS-rplLrplJ). Antisense clones to genes known not to be involved in protein synthesis (atpB/E(AS-atpB/E), visC (AS-visC, *elaD* (AS-*elaD*), yohH (AS-yohH) are much less sensitive to tetracycline.

Definitions

By "biological pathway" is meant any discrete cell function or process that is carried out by a gene product or a subset of gene products. Biological pathways include enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such cell walls. Biological pathways that are usually required for proliferation of microorganisms include, but are not limited to, cell division, DNA synthesis & replication,

RNA synthesis (transcription), protein synthesis (translation), protein processing, protein transport, fatty acid biosynthesis, cell wall synthesis, cell membrane synthesis & maintenance, etc.

By "inhibit activity against a gene or gene product" is meant having the ability to interfere with the function of a gene or gene product in such a way as to decrease expression of the gene or to reduce the level or activity of a product of the gene. Agents which have activity against a gene include agents that inhibit transcription of the gene and agents that inhibit translation of the mRNA transcribed from the gene. In microorganisms, agents which have activity against a gene can act to decrease expression of the operon in which the gene resides or alter the processing of operon RNA such as to reduce the level or activity of the gene product. The gene product can be a non-translated RNA such as ribosomal RNA, a translated RNA (mRNA) or the protein product resulting from translation of the gene mRNA. Of particular utility to the present invention are anti-sense RNAs that have activities against the operons or genes to which they specifically hybridize.

By "activity against a gene product" is meant having the ability to inhibit the function or to reduce the level or activity of the gene product in a cell.

By "activity against a protein" is meant having the ability to inhibit the function or to reduce the level or activity of the protein in a cell.

By "activity against nucleic acid" is meant having the ability to inhibit the function or to reduce the level or activity of the nucleic acid in a cell.

As used herein, "sublethal" means a concentration of an agent below the concentration required to inhibit all cell growth.

DETAILED DESCRIPTION OF THE INVENTION

The present invention describes a group of *E. coli* genes and gene families required for growth and/or proliferation. A proliferation-required gene or gene family is one where, in the absence of a gene transcript and/or gene product, growth or viability of the microorganism is reduced or eliminated. Thus, as used herein the terminology "proliferation-required" or "required for proliferation" encompasses sequences where the absence of a gene transcript and/or gene product completely eliminates cell growth as well as sequences where the absence of a gene transcript and/or gene product merely reduces cell growth. These proliferation-required genes can be used as potential targets for the generation of new antimicrobial agents. To achieve that goal, the present invention also encompasses novel assays for analyzing proliferation-required genes and for identifying compounds which interact with the gene products of the proliferation-required genes. In addition, the present invention contemplates the expression of genes and the purification of the proteins encoded by the nucleic acid sequences identified as required proliferation genes and reported herein. The purified proteins can be used to generate reagents and screen small molecule libraries or other candidate compound libraries for compounds that can be further developed to yield novel antimicrobial compounds. The present invention also describes methods for identification of homologous genes in organisms other than *E. coli*.

The present invention utilizes a novel method to identify proliferation-required *E. coli* sequences. Generally, a library of nucleic acid sequences from a given source are subcloned or otherwise inserted into an inducible expression

vector, thus forming an expression library. Although the insert nucleic acids may be derived from the chromosome of the organism into which the expression vector is to be introduced, because the insert is not in its natural chromosomal location, the insert nucleic acid is an exogenous nucleic acid for the purposes of the discussion herein. The term expression is defined as the production of an RNA molecule from a gene, gene fragment, genomic fragment, or operon. Expression can also be used to refer to the process of peptide or polypeptide synthesis. An expression vector is defined as a vehicle by which a ribonucleic acid (RNA) sequence is transcribed from a nucleic acid sequence carried within the expression vehicle. The expression vector can also contain features that permit translation of a protein product from the transcribed RNA message expressed from the exogenous nucleic acid sequence carried by the expression vector. Accordingly, an expression vector can produce an RNA molecule as its sole product or the expression vector can produce a RNA molecule that is ultimately translated into a protein product.

Once generated, the expression library containing the exogenous nucleic acid sequences is introduced into an *E. coli* population to search for genes that are required for bacterial proliferation. Because the library molecules are foreign to the population of *E. coli*, the expression vectors and the nucleic acid segments contained therein are considered exogenous nucleic acid.

Expression of the exogenous nucleic acid fragments in the test population of *E. coli* containing the expression vector library is then activated. Activation of the expression vectors consists of subjecting the cells containing the vectors to conditions that result in the expression of the exogenous nucleic acid sequences carried by the expression vector library. The test population of *E. coli* cells is then assayed to determine the effect of expressing the exogenous nucleic acid fragments on the test population of cells. Those expression vectors that, upon activation and expression, negatively impact the growth of the *E. coli* screen population were identified, isolated, and purified for further study.

A variety of assays are contemplated to identify nucleic acid sequences that negatively impact growth upon expression. In one embodiment, growth in *E. coli* cultures expressing exogenous nucleic acid sequences and growth in cultures not expressing these sequences is compared. Growth measurements are assayed by examining the extent of growth by measuring optical densities. Alternatively, enzymatic assays can be used to measure bacterial growth rates to identify exogenous nucleic acid sequences of interest. Colony size, colony morphology, and cell morphology are additional factors used to evaluate growth of the host cells. Those cultures that failed to grow or grow with reduced efficiency under expression conditions are identified as containing an expression vector encoding a nucleic acid fragment that negatively affects a proliferation-required gene.

Once exogenous nucleic acid sequences of interest are identified, they are analyzed. The first step of the analysis is to acquire the nucleic acid sequence of the nucleic acid fragment of interest. To achieve this end, the insert in those expression vectors identified as containing a sequence of interest is sequenced, using standard techniques well known in the art. The next step of the process is to determine the source of the nucleic acid sequence.

Determination of sequence source is achieved by comparing the obtained sequence data with known sequences in various genetic databases. The sequences identified are used to probe these gene databases. The result of this

procedure is a list of exogenous nucleic acid sequences corresponding to a list that includes novel bacterial genes required for proliferation as well as genes previously identified as required for proliferation.

The number of DNA and protein sequences available in database systems has been growing exponentially for years. For example, at the end of 1998, the complete sequences of *Caenorhabditis elegans*, *Saccharomyces cerevisiae* and nineteen bacterial genomes, including *E. coli* were available. This sequence information is stored in a number of databanks, such as GenBank (the National Center for Biotechnology Information (NCBI)), and is publicly available for searching.

A variety of computer programs are available to assist in the analysis of the sequences stored within these databases. FastA, (W. R. Pearson (1990) "Rapid and Sensitive Sequence Comparison with FASTP and FASTA" Methods in Enzymology 183:63- 98), Sequence Retrieval System (SRS), (Etzold & Argos, SRS an indexing and retrieval tool for flat file data libraries. Comput. Appl. Biosci. 9:49-57, 1993) are two examples of computer programs that can be used to analyze sequences of interest. In one embodiment of the present invention, the BLAST family of computer programs, which includes BLASTN version 2.0 with the default parameters, or BLASTX version 2.0 with the default parameters, is used to analyze nucleic acid sequences.

BLAST, an acronym for "Basic Local Alignment Search Tool," is a family of programs for database similarity searching. The BLAST family of programs includes: BLASTN, a nucleotide sequence database searching program, BLASTX, a protein database searching program where the input is a nucleic acid sequence; and BLASTP, a protein database searching program. BLAST programs embody a fast algorithm for sequence matching, rigorous statistical methods for judging the significance of matches, and various options for tailoring the program for special situations. Assistance in using the program can be obtained by e-mail at blast@ncbi.nlm.nih.gov.

Bacterial genes are often transcribed in polycistronic groups. These groups comprise operons, which are a collection of genes and intergenic sequences. The genes of an operon are co-transcribed and are often related functionally. Given the nature of the screening protocol, it is possible that the identified exogenous nucleic acid sequence corresponds to a gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation. Accordingly, determining which of the genes that are encoded within the operons are individually required for proliferation is often desirable.

In one embodiment of the present invention, an operon is dissected to determine which gene or genes are required for proliferation. For example, the RegulonDB DataBase described by Huerta et al. (*Nucl. Acids Res.* 26:55-59, 1998), which may also be found on the website http://www.cifn.unam.mx/Computational_Biology/regulondb/, may be used to identify the boundaries of operons encoded within microbial genomes. A number of techniques that are well known in the art can be used to dissect the operon. In one aspect of this embodiment, gene disruption by homologous recombination is used to individually inactivate the genes of an operon that is thought to contain a gene required for proliferation.

Several gene disruption techniques have been described for the replacement of a functional gene with a mutated, non-functional (null) allele. These techniques generally involve the use of homologous recombination. The

method described by Link et al. (J. Bacteriol 1997 179:6228; incorporated herein by reference in its entirety) serves as an excellent example of these methods as applicable to disruption of genes in *E. coli*. This technique uses crossover PCR to create a null allele with an in-frame deletion of the coding region of a target gene. The null allele is constructed in such a way that sequences adjacent to the wild type gene (ca. 500 bp) are retained. These homologous sequences surrounding the deletion null allele provide targets for homologous recombination so that the wild type gene on the *E. coli* chromosome can be replaced by the constructed null allele.

The crossover PCR amplification product is subcloned into the vector pK03, the features of which include a chloramphenicol resistance gene, the counter-selectable marker *sacB*, and a temperature sensitive autonomous replication function. Following transformation of an *E. coli* cell population with such a vector, selection for cells that have undergone homologous recombination of the vector into the chromosome is achieved by growth on chloramphenicol at the non-permissive temperature of 43°C. Under these conditions, autonomous replication of the plasmid cannot occur and cell are resistant to chloramphenicol only if the chloramphenicol resistance gene has been integrated into the chromosome. Usually a single crossover event is responsible for this integration event such that the *E. coli* chromosome now contains a tandem duplication of the target gene consisting of one wild type allele and one deletion null allele separated by vector sequence.

This new *E. coli* strain containing the tandem duplication can be maintained at permissive temperatures in the presence of drug selection (chloramphenicol). Subsequently, cells of this new strain are cultured at the permissive temperature 30°C without drug selection. Under these conditions, the chromosome of some of the cells within the population will have undergone an internal homologous recombination event resulting in removal of the plasmid sequences. Subsequent culturing of the strain in growth medium lacking chloramphenicol but containing sucrose is used to select for such recombinative resolutions. In the presence of the counter-selectable marker *sacB*, sucrose is rendered into a toxic metabolite. Thus, cells that survive this counter-selection have lost both the plasmid sequences from the chromosome and the autonomously replicating plasmid that results as a byproduct of recombinative resolution.

There are two possible outcomes of the above recombinative resolution via homologous recombination. Either the wild type copy of the targeted gene is retained on the chromosome or the mutated null allele is retained on the chromosome. In the case of an essential gene, a single copy of the null allele would be lethal and such cells should not be obtained by the above procedure when applied to essential genes. In the case of a non-essential gene, roughly equal numbers of cells containing null alleles and cells containing wild type alleles should be obtained. Thus, the method serves as a test for essentiality of the targeted gene: when applied to essential genes, only cells with a wild type allele on the chromosome will be obtained.

Other techniques have also been described for the creation of disruption mutations in *E. coli*. For example, Link et al. also describe inserting an in-frame sequence tag concomitantly with an in-frame deletion in order to simplify analysis of recombinants obtained. Further, Link et al. describe disruption of genes with a drug resistance marker such as a kanamycin resistance gene. Arigoni et al., (Arigoni, F. et al. A Genome-based Approach for the

Identification of Essential Bacterial Genes, Nature Biotechnology 16: 851-856, the disclosure of which is incorporated herein by reference in its entirety) describe the use of gene disruption combined with engineering a second copy of a test gene such that the expression of the gene is regulated by and inducible promoter such as the arabinose promoter to test the essentiality of the gene. Many of these techniques result in the insertion of large fragments of DNA into the gene of interest, such as a drug selection marker. An advantage of the technique described by Link et al. is that it does not rely on an insertion into the gene to cause a functional defect, but rather results in the precise removal of the coding region. This insures the lack of polar effects on the expression of genes downstream from the target gene.

Recombinant DNA techniques can be used to express the entire coding sequences of the gene identified as required for proliferation, or portions thereof. The over-expressed proteins can be used as reagents for further study. The identified exogenous sequences are isolated, purified, and cloned into a suitable expression vector using methods well known in the art. If desired, the nucleic acids can contain the sequences encoding a signal peptide to facilitate secretion of the expressed protein.

Expression of fragments of the bacterial genes identified as required for proliferation is also contemplated by the present invention. The fragments of the identified genes can encode a polypeptide comprising at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 75, or more than 75 consecutive amino acids of a gene complementary to one of the identified sequences of the present invention. The nucleic acids inserted into the expression vectors can also contain sequences upstream and downstream of the coding sequence.

When expressing the coding sequence of an entire gene identified as required for bacterial proliferation or a fragment thereof, the nucleic acid sequence to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector can be any of the bacterial, insect, yeast, or mammalian expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon usage and codon bias of the sequence can be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767, incorporated herein by this reference. Fusion protein expression systems are also contemplated by the present invention.

Following expression of the protein encoded by the identified exogenous nucleic acid sequence, the protein is purified. Protein purification techniques are well known in the art. Proteins encoded and expressed from identified exogenous nucleic acid sequences can be partially purified using precipitation techniques, such as precipitation with polyethylene glycol. Chromatographic methods usable with the present invention can include ion-exchange chromatography, gel filtration, use of hydroxyapatite columns, immobilized reactive dyes, chromatofocusing, and use of high-performance liquid chromatography. Electrophoretic methods such one-dimensional gel electrophoresis, high-resolution two-dimensional polyacrylamide electrophoresis, isoelectric focusing, and others are contemplated as purification methods.

Also, affinity chromatographic methods, comprising antibody columns, ligand presenting columns and other affinity chromatographic matrices are contemplated as purification methods in the present invention.

The purified proteins produced from the gene coding sequences identified as required for proliferation can be used in a variety of protocols to generate useful antimicrobial reagents. In one embodiment of the present invention, antibodies are generated against the proteins expressed from the identified exogenous nucleic acid sequences. Both monoclonal and polyclonal antibodies can be generated against the expressed proteins. Methods for generating monoclonal and polyclonal antibodies are well known in the art. Also, antibody fragment preparations prepared from the produced antibodies discussed above are contemplated.

Another application for the purified proteins of the present invention is to screen small molecule libraries for candidate compounds active against the various target proteins of the present invention. Advances in the field of combinatorial chemistry provide methods, well known in the art, to produce large numbers of candidate compounds that can have a binding, or otherwise inhibitory effect on a target protein. Accordingly, the screening of small molecule libraries for compounds with binding affinity or inhibitory activity for a target protein produced from an identified gene sequence is contemplated by the present invention.

The present invention further contemplates utility against a variety of other pathogenic organisms in addition to *E. coli*. For example, the invention has utility in identifying genes required for proliferation in prokaryotes and eukaryotes. For example, the invention has utility with protists, such as *Plasmodium* spp.; plants; animals, such as *Entamoeba* spp. and *Contracaecum* spp; and fungi including *Candida* spp., (e.g., *Candida albicans*), *Saccharomyces cerevisiae*, *Cryptococcus neoformans*, and *Aspergillus fumigatus*. In one embodiment of the present invention, monera, specifically bacteria are probed in search of novel gene sequences required for proliferation. This embodiment is particularly important given the rise of drug resistant bacteria.

The numbers of bacterial species that are becoming resistant to existing antibiotics are growing. A partial list of these organisms includes: *Staphylococcus* spp., such as *S. aureus*; *Enterococcus* spp., such as *E. faecalis*; *Pseudomonas* spp., such as *P. aeruginosa*, *Clostridium* spp., such as *C. botulinum*, *Haemophilus* spp., such as *H. influenzae*, *Enterobacter* spp., such as *E. cloacae*, *Vibrio* spp., such as *V. cholera*; *Moraxala* spp., such as *M. catarrhalis*; *Streptococcus* spp., such as *S. pneumoniae*, *Neisseria* spp., such as *N. gonorrhoeae*; *Mycoplasma* spp., such as *Mycoplasma pneumoniae*; *Salmonella typhimurium*; *Helicobacter pylori*; *Escherichia coli*; and *Mycobacterium tuberculosis*. The sequences identified as required for proliferation in the present invention can be used to probe these and other organisms to identify homologous required proliferation genes contained therein.

In one embodiment of the present invention, the nucleic acid sequences disclosed herein are used to screen genomic libraries generated from bacterial species of interest other than *E. coli*. For example, the genomic library may be from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium*

tuberculosis, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. Standard molecular biology techniques are used to generate genomic libraries from various microorganisms. In one aspect, the libraries are generated and bound to nitrocellulose paper. The identified exogenous nucleic acid sequences of the present invention can then be used as probes to screen the libraries for homologous sequences. The homologous sequences identified can then be used as targets for the identification of new, antimicrobial compounds with activity against more than one organism.

For example, the preceding methods may be used to isolate nucleic acids having a sequence with at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% identity to a nucleic acid sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 1-81, 405-485, 82-88, 90-242, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto. Identity may be measured using BLASTN version 2.0 with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety). For example, the homologous polynucleotides may have a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOS: 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto.

Additionally, the above procedures may be used to isolate nucleic acids which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, or at least 40% identity or similarity to a polypeptide having the sequence of one of SEQ ID NOS: 243-357, 359-398 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety).

Alternatively, homologous nucleic acids or polypeptides may be identified by searching a database to identify sequences having a desired level of homology to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid to a nucleic acid involved in microbial proliferation. A variety of such databases are available to those skilled in the art, including GenBank and GenSeq. In some embodiments, the databases are screened to identify nucleic acids or polypeptides having at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, or at least 50%, at least 40% identity or similarity to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid involved in proliferation. For example, the database may be screened to identify nucleic acids homologous to one of SEQ ID Nos. 1-81, 405-485, 82-88, 90-242 or polypeptides homologous

to SEQ ID NOs. 243-357, 359-398. In some embodiments, the database may be screened to identify homologous nucleic acids or polypeptides from organisms other than *E. coli*, including organisms such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by researchers to help identify optimal drug targets, profile new compounds, and determine disease pathways. An example of this technology is found in U.S. Patent No. 5807522, which is hereby incorporated by reference.

It is possible to study the expression of all genes in the genome of a particular microbial organism using a single array. For example, the arrays from Genosys consist of 12 x 24 cm nylon filters containing PCR products corresponding to 4290 ORFs from *E. coli*. 10 ngs of each are spotted every 1.5 mm on the filter. Single stranded labeled cDNAs are prepared for hybridization to the array (no second strand synthesis or amplification step is done) and placed in contact with the filter. Thus the labeled cDNAs are of "antisense" orientation. Quantitative analysis is done by phosphorimager.

Hybridization of cDNA made from a sample of total cell mRNA to such an array followed by detection of binding by one or more of various techniques known to those in the art results in a signal at each location on the array to which cDNA hybridized. The intensity of the hybridization signal obtained at each location in the array thus reflects the amount of mRNA for that specific gene that was present in the sample. Comparing the results obtained for mRNA isolated from cells grown under different conditions thus allows for a comparison of the relative amount of expression of each individual gene during growth under the different conditions.

Gene expression arrays may be used to analyze the total mRNA expression pattern at various time points after induction of an antisense nucleic acid against a proliferation-required gene. Analysis of the expression pattern indicated by hybridization to the array provides information on whether or not the target gene of the antisense nucleic acid is being affected by antisense induction, how quickly the antisense is affecting the target gene, and for later timepoints, what other genes are affected by antisense expression. For example, if the antisense is directed against a gene for ribosomal protein L7/L12 in the 50S subunit, its targeted mRNA may disappear first and then other mRNAs may be observed to increase, decrease or stay the same. Similarly, if the antisense is directed against a different 50S subunit ribosomal protein mRNA (e.g. L25), that mRNA may disappear first followed by changes in mRNA expression that are similar to those seen with the L7/L12 antisense expression. Thus, the mRNA expression pattern observed

with an antisense nucleic acid against a proliferation required gene may identify other proliferation-required nucleic acids in the same pathway as the target of the antisense nucleic acid. In addition, the mRNA expression patterns observed with candidate drug compounds may be compared to those observed with antisense nucleic acids against a proliferation-required nucleic acid. If the mRNA expression pattern observed with the candidate drug compound is similar to that observed with the antisense nucleic acid, the drug compound may be a promising therapeutic candidate. Thus, the assay would be useful in assisting in the selection of candidate drug compounds for use in screening methods such as those described below.

In cases where the source of nucleic acid deposited on the array and the source of the nucleic acid being hybridized to the array are from two different organisms, gene expression arrays can identify homologous genes in the two organisms.

The present invention also contemplates additional methods for screening other microorganisms for proliferation-required genes. In this embodiment, the conserved portions of sequences identified as proliferation-required can be used to generate degenerate primers for use in the polymerase chain reaction (PCR). The PCR technique is well known in the art. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. This homologous gene is then isolated, expressed, and used as a target for candidate antibiotic compounds. In another aspect of this embodiment, the homologous gene is expressed in an autologous organism or in a heterologous organism in such a way as to alter the level or activity of a homologous gene required for proliferation in the autologous or heterologous organism. In still another aspect of this embodiment, the homologous gene or portion is expressed in an antisense orientation in such a way as to alter the level or activity of a nucleic acid required for proliferation of an autologous or heterologous organism.

The homologous sequences to proliferation-required genes identified using the techniques described herein may be used to identify proliferation-required genes of organisms other than *E. coli*, to inhibit the proliferation of organisms other than *E. coli* by inhibiting the activity or reducing the amount of the identified homologous nucleic acid or polypeptide in the organism other than *E. coli*, or to identify compounds which inhibit the growth of organisms other than *E. coli* as described below.

In another embodiment of the present invention, *E. coli* sequences identified as required for proliferation are transferred to expression vectors capable of function within non-*E. coli* species. As would be appreciated by one of ordinary skill in the art, expression vectors must contain certain elements that are species specific. These elements can include promoter sequences, operator sequences, repressor genes, origins of replication, ribosomal binding sequences, termination sequences, and others. To use the identified exogenous sequences of the present invention, one of ordinary skill in the art would know to use standard molecular biology techniques to isolate vectors containing the sequences of interest from cultured bacterial cells, isolate and purify those sequences, and subclone those sequences into an expression vector adapted for use in the species of bacteria to be screened.

Expression vectors for a variety of other species are known in the art. For example, Cao et al. report the expression of steroid receptor fragments in *Staphylococcus aureus*. J. Steroid Biochem Mol Biol. 44(1):1-11

(1993). Also, Pla et al. have reported an expression vector that is functional in a number of relevant hosts including: *Salmonella typhimurium*, *Pseudomonas putida*, and *Pseudomonas aeruginosa*. *J. Bacteriol.* 172(8):4448-55 (1990). These examples demonstrate the existence of molecular biology techniques capable of constructing expression vectors for the species of bacteria of interest to the present invention.

5 Following the subcloning of the identified nucleic acid sequences into an expression vector functional in the microorganism of interest, the identified nucleic acid sequences are conditionally transcribed to assay for bacterial growth inhibition. Those expression vectors found to contain sequences that, when transcribed, inhibit bacterial growth are compared to the known genomic sequence of the pathogenic microorganism being screened or, if the homologous sequence from the organism being screened is not known, it may be identified and isolated by
10 hybridization to the proliferation-required *E. coli* sequence of interest or by amplification using primers based on the proliferation-required *E. coli* sequence of interest as described above.

 The antisense sequences from the second organism which are identified as described above may then be operably linked to a promoter, such as an inducible promoter, and introduced into the second organism. The techniques described herein for identifying *E. coli* genes required for proliferation may thus be employed to determine
15 whether the identified sequences from a second organism inhibit the proliferation of the second organism.

 Antisense nucleic acids required for the proliferation of organisms other than *E. coli* or the genes corresponding thereto, may also be hybridized to a microarray containing the *E. coli* ORFs to gauge the homology between the *E. coli* sequences and the proliferation-required nucleic acids from other organisms. For example, the proliferation-required nucleic acid may be from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*,
20 *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni* or *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The proliferation-required nucleic acids from an organism other than *E. coli* may be hybridized to the array under a variety of conditions which permit hybridization to occur when the probe has different levels of homology to the sequence on the microarray. This would provide an indication of homology across the organisms as well as clues to other possible essential genes in these organisms.

30 In still another embodiment, the exogenous nucleic acid sequences of the present invention that are identified as required for bacterial growth or proliferation can be used as antisense therapeutics for killing bacteria. The antisense sequences can be directed against the proliferation-required genes whose sequence corresponds to the exogenous nucleic acid probes identified here (i.e. the antisense nucleic acid may hybridize to the gene or a portion thereof). Alternatively, antisense therapeutics can be directed against operons in which proliferation-required genes reside (i.e. the antisense
35 nucleic acid may hybridize to any gene in the operon in which the proliferation-required genes reside). Further, antisense

therapeutics can be directed against a proliferation-required gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation or an operon containing a proliferation-required gene.

In addition to therapeutic applications, the present invention encompasses the use of nucleic acid sequences complementary to sequences required for proliferation as diagnostic tools. For example, nucleic acid probes complementary to proliferation-required sequences that are specific for particular species of microorganisms can be used as probes to identify particular microorganism species in clinical specimens. This utility provides a rapid and dependable method by which to identify the causative agent or agents of a bacterial infection. This utility would provide clinicians the ability to prescribe species specific antimicrobial compounds to treat such infections. In an extension of this utility, antibodies generated against proteins translated from mRNA transcribed from proliferation-required sequences can also be used to screen for specific microorganisms that produce such proteins in a species-specific manner.

The following examples teach the genes of the present invention and a subset of uses for the *E. coli* genes identified as required for proliferation. These examples are illustrative only and are not intended to limit the scope of the present invention.

EXAMPLES

The following examples are directed to the identification and exploitation of *E. coli* genes required for proliferation. Methods of gene identification are discussed as well as a variety of methods to utilize the identified sequences.

Genes Identified as Required for Proliferation of *E. coli*

Exogenous nucleic acid sequences were cloned into an inducible expression vector and assayed for growth inhibition activity. Example 1 describes the examination of a library of exogenous nucleic acid sequences cloned into IPTG-inducible expression vectors. Upon activation or induction, the expression vectors produced an RNA molecule corresponding to the subcloned exogenous nucleic acid sequences. The RNA product was in an antisense orientation with respect to the *E. coli* genes from which it was originally derived. This antisense RNA then interacted with sense mRNA produced from various *E. coli* genes and interfered with or inhibited the translation of the sense messenger RNA (mRNA) thus preventing protein production from these sense mRNA molecules. In cases where the sense mRNA encoded a protein required for the proliferation, bacterial cells containing an activated expression vector failed to grow or grew at a substantially reduced rate.

EXAMPLE 1

Inhibition of Bacterial Proliferation after IPTG induction

To study the effects of transcriptional induction in liquid medium, growth curves were carried out by back diluting cultures 1:200 into fresh media with or without 1 mM IPTG and measuring the OD₄₅₀ every 30 minutes (min). To

study the effects of transcriptional induction on solid medium, 10^2 , 10^3 , 10^4 , 10^5 , 10^6 , 10^7 and 10^8 fold dilutions of overnight cultures were prepared. Aliquots of from 0.5 to 3 μ l of these dilutions were spotted on selective agar plates with or without 1 mM IPTG. After overnight incubation, the plates were compared to assess the sensitivity of the clones to IPTG.

Of the numerous clones tested, some clones were identified as a containing sequence that inhibited *E. coli* growth after IPTG induction. Accordingly, the gene to which the inserted nucleic acid sequence corresponds, or a gene within the operon containing the inserted nucleic acid, may be required for proliferation in *E. coli*.

Characterization of Isolated Clones Negatively Affecting *E. coli* Proliferation

Following the identification of those expression vectors that, upon expression, negatively impacted *E. coli* growth or proliferation, the inserts or nucleic acid fragments contained in those expression vectors were isolated for subsequent characterization. Expression vectors of interest were subjected to nucleic acid sequence determination.

EXAMPLE 2

Nucleic Acid Sequence Determination of Identified Clones Expressing Nucleic Acid Fragments with Detrimental Effects of *E. coli* Proliferation

The nucleotide sequences for the exogenous identified sequences were determined using plasmid DNA isolated using QIAPREP (Qiagen, Valencia, CA) and methods supplied by the manufacturer. The primers used for sequencing the inserts were 5' - TGTTTATCAGACCGCTT - 3' (SEQ ID NO: 403) and 5' - ACAATTTACACAGCCTC - 3' (SEQ ID NO: 404). These sequences flank the polylinker in pLEX5BA. Sequence identification numbers (SEQ ID NOs) for the identified inserts are listed in Table I and discussed below.

EXAMPLE 3

Comparison Of Isolated Sequences to Known Sequences

The nucleic acid sequences of the subcloned fragments obtained from the expression vectors discussed above were compared to known *E. coli* sequences in GenBank using BLAST version 1.4 or version 2.0.6 using the following default parameters: Filtering off, cost to open a gap=5, cost to extend a gap=2, penalty for a mismatch in the blast portion of run=-3, reward for a match in the blast portion of run=1, expectation value (e)=10.0, word size=11, number of one-line descriptions=100, number of alignments to show (B)=100. BLAST is described in Altschul, J Mol Biol. 215:403-10 (1990), the disclosure of which is incorporated herein by reference in its entirety. Expression vectors were found to contain nucleic acid sequences in both the sense and antisense orientations. The presence of known genes, open reading frames, and ribosome binding sites was determined by comparison to public databases holding genetic information and various computer programs such as the Genetics Computer Group programs FRAMES and CODONPREFERENCE. Clones were designated as "antisense" if the cloned fragment was oriented to the promoter such that the RNA transcript produced was complementary to the expressed mRNA from a chromosomal locus. Clones were designated as "sense" if they coded for an RNA fragment that was identical to a portion of a wild type mRNA from a chromosomal locus.

The sequences described in Examples 1-2 that inhibited bacterial proliferation and contained gene fragments in an antisense orientation are listed in Table I. This table lists each identified sequence by: a sequence identification number; a Molecule Number; a gene to which the identified sequence corresponds, listed according to the National Center for Biotechnology Information (NCBI), Blattner (Science 277:1453-1474(1997); also contains the *E. coli* K-12 genome sequence), or Rudd (Micro. and Mol. Rev. 62:985-1019 (1998)), (both papers are hereby incorporated by reference) nomenclatures. The CONTIG numbers for each identified sequence is shown, as well as the location of the first and last base pairs located on the *E. coli* chromosome. A Molecule Number with a "*" indicates a clone corresponding to an intergenic sequence.

The sequences of the nucleic acid inserts of SEQ ID NOs: 1-81 from U.S. Provisional Patent Application No. 60/117,405 which inhibited proliferation were further analyzed. The reanalyzed sequences corresponding to SEQ ID NOs. 1-81 of U.S. Provisional Patent Application No. 60/117,405 have SEQ ID NOs. 405-485 in the present application.

SEQ ID NOs: 82-242 in U.S. Provisional Patent Application No. 60/117,405 are identical to SEQ ID NOs: 82-242 of the present application with the following exceptions. SEQ ID NO: 148 in the present application is the complementary strand of SEQ ID NO: 148 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 308 which is encoded by SEQ ID NO: 148 has also been revised. SEQ ID NO: 163 in the present application is the complementary strand of SEQ ID NO: 163 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 323 which is encoded by SEQ ID NO: 163 has also been revised.

The target gene of SEQ ID NOs. 18 and 19 of U.S. Provisional Patent Application No. 60/117,405 (SEQ ID NOs. 18, 19, 422, 423 of the present application) has been revised from *dicF* to *ftsZ* to reflect the fact that these SEQ ID NOs. include natural antisense molecules which inhibit *ftsZ* expression.

The gene products of the nucleic acids of SEQ ID NOs. 198 and 239-242 in U.S. Provisional Patent Application No. 60/117,405 and in the present application (SEQ ID NOs. 358 and 399-402 of the present application) have been revised to reflect the fact that these nucleic acids encode nontranslated tRNAs and rRNAs. Tables I and II have been revised accordingly. The SEQ ID NOs. in Table II were also revised to reflect the fact that SEQ ID NOs: 89 and 402 were identical in U.S. Provisional Patent Application No. 60/117,405.

TABLE I

Identified Clones with Corresponding Genes and Operons

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
1, 405	EcXA001	<i>yhhQ</i>	<i>b3471</i>	<i>yhhQ</i>	AE000423
2, 406	EcXA002	<i>lepB</i>	<i>lepB</i>	<i>lepB</i>	AE000343
3, 407	EcXA003	<i>f586</i>	<i>b0955</i>	<i>ycbZ</i>	AE000197
4, 408	EcXA004	<i>rpsG, rpsL</i>	<i>b3341</i>	<i>rpsG, rpsL</i>	AE000410
5, 409	EcXA005a	<i>rplL, rplJ</i>	<i>b3986</i>	<i>rplL, rplJ</i>	AE000472
6, 410	EcXA005b	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
7, 411	EcXA005c	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
8, 412	EcXA005d	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
9, 413	EcXA005e	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
10, 414	EcXA005f	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
11, 415	EcXA005g	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
12, 416	EcXA006	<i>pta</i>	<i>b2297</i>	<i>pta</i>	AE000319
13, 417	EcXA007	<i>yicP</i>	<i>b3666</i>	<i>yicP</i>	AE000444
14, 418	EcXA008a	<i>yhaU</i>	<i>b3127</i>	<i>yhaU</i>	AE000394
15, 419	EcXA008b	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
16, 420	EcXA008c	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
17, 421	EcXA009	<i>ydeY</i>	<i>ydeY</i>	<i>ydeY</i>	AE000249
18, 422	EcXA010a (natural as)	<i>dicF</i>	<i>b1575</i>	<i>dicF</i>	AE000253
19, 423	EcXA010b	<i>dicF</i>	<i>dicF</i>	<i>dicF</i>	AE000253
20, 424	EcXA011	<i>fdnG</i>	<i>b1474</i>	<i>fdnG</i>	AE000244
21, 425	EcXA012a	<i>fusA</i>	<i>b3340</i>	<i>fusA</i>	AE000410
22, 426	EcXA012b	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
23, 427	EcXA012c	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
24, 428	EcXA013a	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
25, 429	EcXA013b	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
26, 430	EcXA013c	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
27, 431	EcXA014	<i>visC</i>	<i>b2906</i>	<i>visC</i>	AE000374
28, 432	EcXA015	<i>yfdI</i>	<i>yfdI</i>	<i>yfdI</i>	AE000323
29, 433	EcXA016	<i>yeaQ</i>	<i>yeaQ</i>	<i>yeaQ</i>	AE000274
		<i>yoaG</i>	<i>yoaG</i>	<i>yoaG</i>	
30, 434	EcXA017a	<i>yggE</i>	<i>b2922</i>	<i>yggE</i>	AE000375
31, 435	EcXA017b	<i>yggE</i>	<i>yggE</i>	<i>yggE</i>	AE000375
32, 436	EcXA018a	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
33, 437	EcXA018b	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
34, 438	EcXA019a	<i>yehA</i>	<i>yehA</i>	<i>yehA</i>	AE000300
					AE000299
35, 439	EcXA019b	<i>o172, yehA</i>	<i>o172, yehA</i>	<i>o172, yehA</i>	AE000299
36, 440	EcXA020	<i>o384, f82</i>	<i>b1794, b1795</i>	<i>yeaP, yeaQ</i>	AE000274
37, 441	EcXA021a	<i>f112</i>	<i>b0218</i>	<i>yafU</i>	AE000130
38, 442	EcXA021b	<i>f112</i>	<i>b0218</i>	<i>yafU</i>	AE000130
39, 443	EcXA022	<i>o740</i>	<i>b1629</i>	<i>ydqN</i>	AE000258
40, 444	EcXA023a	<i>f176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
41, 445	EcXA023b	<i>f176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
42, 446	EcXA024	<i>ygiM, ygiN</i>	<i>b3082</i>	<i>ygiM, ygiN</i>	AE000390
43, 447	EcXA025	<i>O2383</i>	<i>b1878</i>	<i>yeaJ</i>	AE000289
44, 448	EcXA026	<i>o61</i>	<i>Unpre-dicted</i>	<i>Unpre-dicted</i>	AE000138
45, 449	EcXA027a	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
46, 450	EcXA027b	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
47, 451	EcXA027c	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
		<i>yohI</i>	<i>yohI</i>	<i>yohI</i>	
48, 452	EcXA027d	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
49, 453	EcXA028	<i>f296</i>	<i>b2305</i>	<i>yfcI</i>	AE000319
50, 454	EcXA029	<i>yjiK</i>	<i>b4391</i>	<i>yjiK</i>	AE000509
51, 455	EcXA030	<i>yi5A</i>	<i>b3557</i>	<i>yi5A</i>	AE000433
52, 456	EcXA031	<i>rplE</i>	<i>B3308</i>	<i>rplE</i>	AE000408
53, 457	EcXA032a	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175
54, 458	EcXA032b**	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
		<i>gltA</i>	<i>gltA</i>	<i>gltA</i>	
55, 459	EcXA033a	<i>f477 (as)</i>	<i>b3052</i>	<i>waaE</i>	AE000387
					AE000386
56, 460	EcXA033b	<i>f477</i>	<i>b3052</i>	<i>waaE</i>	AE000387
57, 461	EcXA034a	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
58, 462	EcXA034b	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
59, 463	EcXA035	<i>yhjU</i>	<i>yhjU</i>	<i>yhjU</i>	AE000431
60, 464	EcXA036	<i>yqiF</i>	<i>b3101</i>	<i>yqiF</i>	AE000392
		<i>o99</i>	<i>b3100</i>	<i>yqiK</i>	
61, 465	EcXA037	<i>ydeH</i>	<i>b1535</i>	<i>ydeH</i>	AE000251
62, 466	EcXA038	<i>sieB</i>	<i>b1353</i>	<i>sieB</i>	AE000233
63, 467	EcXA039	<i>ybbD</i>		<i>ybbD</i>	AE000156
64, 468	EcXA040	<i>insB 6</i>	<i>b3445</i>	<i>insB 6</i>	AE000420
65, 469	EcXA041	<i>f234</i>	<i>b1138</i>	<i>ymtE</i>	AE000214
66, 470	EcXA042a	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
67, 471	EcXA042b	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
68, 472	EcXA043	<i>ybgB</i>	<i>ybgB</i>	<i>ybgB</i>	AE000176
		<i>cydA</i>	<i>cydA</i>	<i>cydA</i>	
69, 473	EcXA044	<i>purB</i>	<i>b1131</i>	<i>purB</i>	AE000213
70, 474	EcXA045**	<i>csrA</i>	<i>csrA</i>	<i>csrA</i>	AE000353
		<i>serV</i>	<i>serV</i>	<i>serV</i>	
71, 475	EcXA046**	<i>fimE, fimA</i>	<i>b4313</i>	<i>fimE, fimA</i>	AE000502
72, 476	EcXA047**	<i>f96, cspB</i>	<i>f96, cspB</i>	<i>cspB, ydfS</i>	AE000252
73, 477	EcXA048	<i>yefE</i>	<i>yefE</i>	<i>yefE</i>	AE000294
74, 478	EcXA049	<i>yaiC</i>	<i>b0385</i>	<i>yaiC</i>	AE000145
75, 479	EcXA050	<i>o467, o222</i>	<i>yaiU, yaiV</i>	<i>yaiU, yaiV</i>	AE000144
76, 480	EcXA051a	<i>rplB, rplW</i>	<i>rplB, rplW</i>	<i>rplB, rplW</i>	AE000408
77, 481	EcXA051b	<i>rplW</i>	<i>rplW</i>	<i>rplW</i>	AE000408
78, 482	EcXA052	<i>infC</i>	<i>infC</i>	<i>infC</i>	AE000267
					AE000266
79, 483	EcXA053	<i>gor</i>	<i>gor</i>	<i>gor</i>	AE000426
80, 484	EcXA054	<i>rplF</i>	<i>rplF</i>	<i>rplF</i>	AE000408
81, 485	EcXA055	<i>rrlG</i>	<i>rrlG</i>	<i>rrlG</i>	AE000345

EXAMPLE 4

Identification of Genes and their Corresponding Operons Affected by Antisense Inhibition

The sequencing of the entire *E. coli* genome is described in Blattner et al., Science 277:1453-1474(1997) the entirety of which is hereby incorporated by reference and the sequence of the genome is listed in GenBank Accession No.U00096, the disclosure of which is incorporated herein by reference in its entirety. The operons to which the proliferation-inhibiting nucleic acids correspond were identified using RegulonDB and information in the literature. The coordinates of the boundaries of these operons on the *E. coli* genome are listed in Table III. Table II lists the molecule numbers of the inserts containing the growth inhibiting nucleic acid fragments, the genes in the operons corresponding to the inserts, the SEQ ID NOs of the genes containing the inserts, the SEQ ID NOs of the proteins encoded by the genes, the start and stop points of the genes on the *E. coli* genome, the orientation of the genes on the genome, whether the operons

are predicted or documented, and the predicted functions of the genes. The identified operons, their putative functions, and whether or not the genes are presently thought to be required for proliferation are discussed below.

Functions for the identified genes were determined by using either Blattner functional class designations or by comparing identified sequence with known sequences in various databases. A variety of biological functions were noted for the genes to which the clones of the present invention correspond. The functions for the genes of interest appear in Table II.

The proteins that are listed in Table II are involved in a wide range of biological functions.

TABLE II
All Operon Data with Whole Chromosome Coordinates

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
82	243	EcXA001	<i>yhhQ</i>	3606848	3607513	(P)	Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
83	244		<i>dcbB</i>	3607532	3608143		Hypothetical ORF, unclassified, unknown	Resistance to phage C1; periplasmic protein perhaps anchored to inner membrane
84	245	EcXA002	<i>lepB</i>	2702355	2703329	(P)	Transport and binding proteins	Secretion
85	246	EcXA003	<i>ycbZ</i>	1015762	1017522	(P)	Unknown	Protease
86	247	EcXA004	<i>tufA</i>	3467782	3468966	(D)	Translation, post-translational modification	Translation (Elongation factor Tu)
87	248		<i>fusA</i>	3469037	3471151		Translation, post-translational modification	Translation (elongation factor efg)
88	249		<i>rpsG</i>	3471179	3471718		Translation, post-translational modification	Translation
89	402	EcXA055	<i>rrsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)
90	250		<i>rpsL</i>	3471815	3471815		Translation, post-translational modification	Translation
91	251	EcXA005a-g	<i>rplJ</i>	4177574	4178071	(D)	Translation, post-translational modification	Translation
92	252		<i>rplL</i>	4178138	4178503		Translation, post-translational modification	Translation
93	253	EcXA006	<i>pta</i>	2412767	2414911	(P)	Carbon compound catabolism	Carbon compound catabolism
94	254	EcXA007	<i>yicP</i>	3841591	3943357	(P)	Hypothetical ORF, unclassified, unknown	Probable adenine deaminase

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
95	255	EcXA008a-c	<i>yhaD</i>	3268266	3269492	(P)	Hypothetical ORF, unclassified, unknown	
96	256		<i>yhaE</i>	3269508	3270407		Putative enzymes	
97	257		<i>yhaF</i>	3270428	3271198		Hypothetical ORF, unclassified, unknown	
98	258		<i>yhaU</i>	3271214	3272548		Carbon compound catabolism	Probable integral membrane protein Phthalate permease family
99	259	EcXA009	<i>ydeX</i>	1599514	1601049	(P)	Putative transport proteins	
100	260		<i>ydeY</i>	1601043	1602071		Putative transport proteins	Putative ABC transporter
101	261		<i>ydeZ</i>	1602071	1603063		Hypothetical ORF, unclassified, unknown	
102	262		<i>yneA</i>	1603075	1604097		Hypothetical ORF, unclassified, unknown	
103	263		<i>yneB</i>	1604124	1604999		Hypothetical ORF, unclassified, unknown	
104	264		<i>yneC</i>	1605023	1605313		Hypothetical ORF, unclassified, unknown	
105	265	EcXA010a-b	<i>ftsZ</i>	105305	106456	(P)	Cell processes (incl. Adaptation, protection)	Regulator of cell division
106	266	EcXA011	<i>fdnG</i>	1545425	1548472	(D)	Energy metabolism	Anaerobic respiration (formate dehydro-genase)
107	267		<i>fdnH</i>	1548485	1549369		Energy metabolism	
108	268	EcXA 012a-c	<i>fdnI</i>	1549362	1550015		Energy metabolism	
			Same operon as EcXA004					
109	269	EcXA013a-c	<i>yhlL</i>	2697683	2697943	(P)	Hypothetical ORF, unclassified, unknown	No homologues, no motifs
110	270	EcXA014	<i>visC</i>	3049135	3050337	(P)	Hypothetical ORF, unclassified, unknown	Ubiquinone synthesis

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
111	271		<i>ubiH</i>	3050360	3051538		Biosynthesis of cofactors, prosthetic groups and carriers	
112	272		<i>pepP</i>	3051535	3052860		Translation, post-translational modification	
113	273		<i>ygiB</i>	3052886	3053470		Hypothetical ORF, unclassified, unknown	
114	274	EcXA015	<i>yfdG</i>	2465875	2466237	(P)	Hypothetical ORF, unclassified, unknown	
115	275		<i>yfdH</i>	2466234	2467154		Cell structure	
116	276		<i>yfdI</i>	2467151	2468482		Hypothetical ORF, unclassified, unknown	Putative membrane protein
117	277	EcXA016	<i>yeaQ</i>	1877031	1877279	(P)	Hypothetical ORF, unclassified, unknown	Homologue to transglycosylase associated protein
118	278		<i>yeaG</i>	1877427	1877609	(P)	Hypothetical ORF, unclassified, unknown	No homologues
119	279		<i>yeaR</i>	1877613	1877972		Hypothetical ORF, unclassified, unknown	
120	280	EcXA017a-b	<i>yggE</i>	3065360	3066100	(P)	Structural proteins	Homologues in multiple bacteria, no motifs
121	281	EcXA018a-b	<i>yegM</i>	2151891	2153285	(P)	Putative transport proteins	Transport (multiple transferable resistance)
122	282		<i>yegN</i>	2153285	2156407		Hypothetical ORF, unclassified, unknown	
123	283		<i>yegO</i>	2156408	2159485		Hypothetical ORF, unclassified, unknown	
124	284		<i>yegB</i>	2159486	2160901		Putative transport proteins	
125	285	EcXA019a-b	<i>yehA</i>	2185400	2186434	(P)	Cell structure	Weak homology to pilin precursor from <i>H. Inf.</i>

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
126	286		<i>yehB</i>	2186450	2188930		Hypothetical ORF, unclassified, unknown	
127	287		<i>yehC</i>	2188946	2189665		Putative chaperones	
128	288		<i>yehD</i>	2189700	2190242		Cell structure	
		EcXA020	Same operon as EcXA016 (one of the two)					
129	289	EcXA021a-b	<i>yafU</i>	238746	239084	(P)	Hypothetical ORF, unclassified, unknown	Homologues in <i>H. Inf.</i> and <i>S. Pombe.</i> , no motifs, transmembrane region present
130	290	EcXA022	<i>ydgL</i>	1703791	1704372	(P)	Hypothetical ORF, unclassified, unknown	
131	291		<i>ydgM</i>	1704372	1704950		Hypothetical ORF, unclassified, unknown	
132	292		<i>ydgN</i>	1704943	1707165		Hypothetical ORF, unclassified, unknown	
133	293		<i>ydgO</i>	1707166	1708224		Hypothetical ORF, unclassified, unknown	
134	294		<i>ydgP</i>	1708228	1708848		Hypothetical ORF, unclassified, unknown	
135	295		<i>ydgQ</i>	1708852	1709547		Hypothetical ORF, unclassified, unknown	
136	296		<i>nth</i>	1709547	1710182		Transcription, RNA processing and degradation	
137	297	EcXA023a-b	<i>ydeR</i>	1585817	1586320	(P)	Hypothetical ORF, unclassified, unknown	
138	298		<i>ydeS</i>	1586333	1586863		Hypothetical ORF, unclassified, unknown	fimf-like

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
139	299		<i>ydeI</i>	1586877	1588025		Structural proteins	find-like
140	300	EcXA024	<i>ygiM</i>	3231369	3231785	(P)	Hypothetical ORF, unclassified, unknown	Weak homology to long chain fatty acid coa ligase in <i>Archaeoglobus</i>
141	301		<i>ygiN</i>	3231782	3232096		Hypothetical ORF, unclassified, unknown	Homologues in various bacteria
142	302	EcXA025	<i>yeeJ</i>	2042885	2050036	(P)	Hypothetical ORF, unclassified, unknown	Strong similarity to numerous attaching and effacing proteins and invasins
143	303	EcXA026	<i>yajA</i>	331001	331184	unpredicted		nifm like
144	304	EcXA027a-d	<i>yohG</i>	2225343	2226539	(P)	Putative transport proteins	
145	305		<i>yohH</i>	2226569	2226859		Hypothetical ORF, unclassified, unknown	Xylose binding protein-like
146	306		<i>yohI</i>	2227458	2228405	(P)	Putative regulatory protein	
147	307	EcXA028	<i>yclI</i>	2420669	2421559	(P)	Hypothetical ORF, unclassified, unknown	Similar to <i>S. Typhi</i> histidine transport gene
148	308	EcXA029	<i>yjiK</i>	4626424	4628091	(P)	Hypothetical ORF, unclassified, unknown	Similar to ABC transporter
149	309	EcXA030	<i>yi5A</i>	3718309	3718830	(P)	Hypothetical ORF, unclassified, unknown	IS150 orf A
150	310		<i>yi5B</i>	3718827	3719678		Phage, transposon, or plasmid	
151	311	EcXA031	<i>rpmJ</i>	3440255	3440371	(D)	Translation, post-translational modification	
152	312		<i>priA</i>	3440403	3441734		Putative transport proteins	
153	313		<i>rpI0</i>	3441742	3442176		Translation, post-translational modification	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
154	314		<i>rpmD</i>	3442180	3442359		Translation, post-translational modification	
155	315		<i>rpsE</i>	3442363	3442866		Translation, post-translational modification	
156	316		<i>rplR</i>	3442881	3443234		Translation, post-translational modification	
157	317		<i>rplF</i>	3443244	3443777		Translation, post-translational modification	Translation
158	318		<i>rpsH</i>	3443790	3444182		Translation, post-translational modification	
159	319		<i>rpsN</i>	3444216	3444521		Translation, post-translational modification	
160	320		<i>rplE</i>	3444536	3445075		Translation, post-translational modification	Translation
161	321		<i>rplX</i>	3445090	3445404		Translation, post-translational modification	
162	322		<i>rplN</i>	3445415	3445786		Translation, post-translational modification	
163	323	EcXA032a-b	<i>ybgD</i>	751452	752018	(P)	Cell processes (incl. Adaptation, protection)	Hypothetical fimbrial protein
164	324		<i>gluA</i>	752408	753691	(D)	Energy metabolism	Glutamine biosynthesis
165	325	EcXA033a-b	<i>waeE</i>	3192961	3194394	(P)	Putative enzymes	ADP heptose synthase/ autotrophic growth protein
166	326		<i>glnE</i>	3194442	3197282		Translation, post-translational modification	
167	327		<i>ygiF</i>	3197305	3198606		Hypothetical ORF, unclassified, unknown	
168	328	EcXA034a-b	<i>cspA</i>	3717678	3717890	(P)	Cell processes (incl. Adaptation, protection)	RNA chaperonin
169	329	EcXA035	<i>yhjS</i>	3694087	3695658	(P)	Translation, post-translational modification	

GeneSeq ID No.	Gene Prod. Seq ID No.	Note. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
170	330		<i>yhjT</i>	3695658	3695846		Hypothetical ORF, unclassified, unknown	
171	331		<i>yhjU</i>	3695843	3697522		Hypothetical ORF, unclassified, unknown	Regions similar to dehydrogenases, nucleases etc.
172	332	EcXA036	<i>yqjC</i>	3246594	3246977	(P)	Hypothetical ORF, unclassified, unknown	
173	333		<i>yqjD</i>	3247015	3247320		Hypothetical ORF, unclassified, unknown	
174	334		<i>yqjE</i>	3247323	3247727		Hypothetical ORF, unclassified, unknown	
175	335		<i>yqjK</i>	3247717	3248016		Similar to mukb from H. Inf.	
176	336		<i>yqjF</i>	3248112	3248594	(P)	Hypothetical ORF, unclassified, unknown	Homologues in many bacteria; blocks; secretion/ATP synthase/ftsZ
177	337	EcXA037	<i>ydeH</i>	1620984	1621874	(P)	Hypothetical ORF, unclassified, unknown	Similar to carboxy-kinase, oxidase, symporters
178	338	EcXA038	<i>sieB</i>	1416572	1417183	(P)	Phage, transposon, or plasmid	Super-infection exclusion factor B-like
179	339		<i>rajB (b1354)</i>	1417192	1417368		Hypothetical ORF, unclassified, unknown	
180	340	EcXA039	<i>rhsD</i>	522485	526765	(P)	Hypothetical ORF, unclassified, unknown	
181	341		<i>ybaC</i>	526805	527173		Hypothetical ORF, unclassified, unknown	
182	342		<i>ybhH</i>	527173	527883		Hypothetical ORF, unclassified, unknown	Rhs-like element
183	343		<i>ybdD</i>	527864	528124		Hypothetical ORF, unclassified, unknown	ATP synthase, desaturase

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
184	344		<i>ybl</i>	528163	528354		Hypothetical ORF, unclassified, unknown	
185	345	EcXA040	<i>insB_6</i>	351114	351389	(P)	Phage, transposon, or plasmid	
186	346		<i>insA</i>	351308	3581811		Phage, transposon, or plasmid	
187	347		<i>yrhA</i>	3580669	3581085		Hypothetical ORF, unclassified, unknown	
188	348		<i>yhhZ</i>	3579494	3580672		Hypothetical ORF, unclassified, unknown	
189	349	EcXA041	<i>ymfD</i>	1196090	1196755	(P)	Hypothetical ORF, unclassified, unknown	No assigned role
190	350		<i>ymfE</i>	1196756	1197460		Hypothetical ORF, unclassified, unknown	No assigned role
191	351	EcXA042a-b	<i>rplY</i>	2280537	2280821	(P)	Translation, post-translational modification	Translation
192	352	EcXA043	<i>hrsA</i>	765207	767183	(P)	Translation, post-translational modification	
193	353		<i>yhgB</i>	767201	769834		Carbon compound catabolism	Unknown
194	354		<i>cydA</i>	770678	772249	(D)	Energy metabolism	Cytochrome D oxidase
195	355		<i>cydB</i>	772265	773404		Energy metabolism	
196	356	EcXA044	<i>purB</i>	1189839	1191209	(D)	Nucleotide biosynthesis and metabolism	Purine biosynthesis
197	357	EcXA045	<i>csrA</i>	2816983	2817168	(P)	Regulatory function	Carbon storage regulator (mRNA decay factor)
198	358		<i>serV</i>	2816575	2816667	Unpredicted	Translation, post-translational modification	Translation (tRNA)
199	359	EcXA046	<i>fimB</i>	4538525	4539127	(D)	Cell structure	
200	360		<i>fimE</i>	4539605	4540201		Cell structure	Fimbriae
201	361		<i>fimA</i>	4540683	4541231		Cell structure	Regulator of inversion

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
202	362		<i>fimI</i>	4541188	4541835		Cell structure	
203	363		<i>fimC</i>	4541872	4542597		Cell structure	
204	364		<i>fimD</i>	4542665	4545301		Cell structure	
205	365		<i>fimF</i>	4545311	4545841		Cell structure	
206	366		<i>fimG</i>	4545854	4546357		Cell structure	
207	367		<i>fimH</i>	4546377	4547279		Cell structure	
208	368	EcXA047	<i>ydiP</i>	1637054	1638684	(P)	Hypothetical ORF, unclassified, unknown	
209	369		<i>ydiQ</i>	1637548	1638081		Hypothetical ORF, unclassified, unknown	
210	370		<i>ydiR</i>	1638078	1638389		Hypothetical ORF, unclassified, unknown	
211	371		<i>ydiS</i>	1638394	1638684		Hypothetical ORF, unclassified, unknown	Lysis protein
212	372		<i>cspB</i>	1639363	1639578	(P)	Cell processes (incl. Adaptation, protection)	
213	373	EcXA048	<i>yf52_7</i>	2099917	2100933	(P)	Phage, transposon, or plasmid	
214	374		<i>yefJ</i>	2100938	2101411		Putative enzymes	
215	375		<i>yefI</i>	2101413	2102531		Hypothetical ORF, unclassified, unknown	
216	376		<i>yefH</i>	2102516	2103106		Putative enzymes	
217	377		<i>yefG</i>	2103087	2104079		Hypothetical ORF, unclassified, unknown	
218	378		<i>rfc</i>	2104082	2105248		Cell structure	
219	379		<i>yefE</i>	2105248	2106351		Hypothetical ORF, unclassified, unknown	UDP galacto-pyranase mutase
220	380	EcXA049	<i>yaiC</i>	402927	404042	(P)	Hypothetical ORF, unclassified, unknown	Unknown
221	381	EcXA050	<i>yaiU</i>	392239	393642	(P)	Putative enzymes	Putative auto-transporter

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
222	382		<i>yaiV</i>	393685	394353		Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
223	383	EcXA051a-b	<i>rpsQ</i>	3445951	3446205	(D)	Translation, post-translational modification	
224	384		<i>rpmC</i>	3446205	3446396		Translation, post-translational modification	
225	385		<i>rplP</i>	3446396	3446806		Translation, post-translational modification	
226	386		<i>rpsC</i>	3446819	3447520		Translation, post-translational modification	
227	387		<i>rplV</i>	3447538	3447870		Translation, post-translational modification	
228	388		<i>rpsS</i>	3447885	3448163		Translation, post-translational modification	
229	389		<i>rplB</i>	3448180	3449001		Translation, post-translational modification	Translation
230	390		<i>rplW</i>	3449019	3449321		Translation, post-translational modification	Translation
231	391		<i>rplD</i>	3449318	3449923		Translation, post-translational modification	
232	392		<i>rplC</i>	3449934	3450563		Translation, post-translational modification	
233	393		<i>rpsJ</i>	3450596	3450907		Translation, post-translational modification	
234	394	EcXA052	<i>rplT</i>	1797417	1797773	(D)	Translation, post-translational modification	
235	395		<i>rplM</i>	1797826	1798023		Translation, post-translational modification	
236	396		<i>infC</i>	1798120	1798662		Translation, post-translational modification	Translation

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
237	397		<i>thrS</i>	1798666	1800594		Translation, post-translational modification	
238	398	EcXA053	<i>gor</i>	3643929	3645281	(P)	Biosynthesis of cofactors, prosthetic groups and carriers	Glutathione oxido-reductase
		EcXA054	Same operon as EcXA031					
239	399	EcXA055	<i>rrfG</i>	2724301	2727204	(D)	Translation, post-translational modification	Translation (rRNA)
240	400		<i>rrfG</i>	2724089	2724208		Translation, post-translational modification	Translation (rRNA)
241	401		<i>gltW</i>	2727389	2727464		Translation, post-translational modification	Translation (tRNA)
242	402		<i>rnsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)

Several of the expression vectors contain fragments that correspond to genes of unknown function or if the function is known, it is not known whether the gene is essential. For example, EcXA001, 003, 007, 008, 013, 015, 016, 017, 018, 019, 020, 021, 022, 023, 024, 025, 026, 027, 028, 029, 030, 032, 033, 034, 035, 036, 037, 038, 039, 040, 041, 047, 048, 049 and 050 are all exogenous nucleic acid sequences that correspond to *E. coli* proteins that have no known function or where the function has not been shown to be essential or nonessential.

The present invention reports a number of novel *E. coli* genes and operons that are required for proliferation. From the list clone sequences identified here, each was identified to be a portion of a gene in an operon required for the proliferation of *E. coli*. Cloned sequences corresponding to genes already known to be required for proliferation in *E. coli* include EcXA002, 004, 005, 010, 012, 014, 031, 02, 043, 045, 051, 052, 054, and 055. The remaining identified sequences correspond to *E. coli* genes previously undesignated as required for proliferation in the art.

An interesting observation of the present invention is that there are also several sequence fragments that correspond to *E. coli* genes that are not thought to be required for *E. coli* proliferation. Nevertheless, under the conditions described above, the antisense expression of these gene fragments causes a reduction in cell growth. This result implies that the genes corresponding to the identified sequences are actually required for proliferation. Molecule Nos. corresponding to these genes are EcXA006, 044, 046, and 053.

Following identification of the sequences of interest, these sequences were localized into operons. Since bacterial genes are expressed in a polycistronic manner, the antisense inhibition of a single gene in an operon might effect the expression of all the other genes on the operon or the genes down stream from the single gene identified. In order to determine which of the gene products in an operon are required for proliferation, each of the genes contained within an operon may be analyzed for their effect on viability as described below.

TABLE III
Operon Boundaries

Mole. No.	Left Coordinate	Right Coordinate
EcXA001	3606848	3608143
EcXA002	2702355	2703329
EcXA003	1015762	1017522
EcXA004	3467782	3472189
EcXA005	4177574	4178503
EcXA006	2412767	2414911
EcXA007	3841591	3843357
EcXA008	3268266	3272548
EcXA009	1599514	1605313
EcXA010	1647406	1647458
EcXA011	1545425	1550015
EcXA012	3467782	3472189
EcXA013	2697683	2697943
EcXA014	3049135	3053470
EcXA015	2465875	2468482
EcXA016	1877031	1877972
EcXA017	3065360	3066100
EcXA018	2151891	2160901
EcXA019	2185400	2190242
EcXA020	1877031	1877972
EcXA021	238746	239084
EcXA022	1703791	1710182
EcXA023	1585817	1588025
EcXA024	3231369	3232096
EcXA025	2042885	2050036
EcXA026	331001	331184
EcXA027c	2225343	2228405
EcXA028	2420669	2421559
EcXA029	4626424	4628091
EcXA030	3718309	3719678
EcXA031	3440255	3445786
EcXA032b	751452	753691
EcXA033	3192961	3198606
EcXA034	3717678	3717890
EcXA035	3694087	3697522
EcXA036	3246594	3248594
EcXA037	1620984	1621874
EcXA038	1416572	1417368
EcXA039	522485	528354
EcXA040	3580669	3580672
EcXA041	1196090	1197460
EcXA042	2280537	2280821

Mole. No.	Left Coordinate	Right Coordinate
EcXA043	765207	773404
EcXA044	1189839	1191209
EcXA045	2816575	2817168
EcXA046	4538525	4547279
EcXA047	1637054	1639578
EcXA048	2099917	2106351
EcXA049	402927	404042
EcXA050	392239	394353
EcXA051	3445951	3450907
EcXA052	1797417	1800594
EcXA053	3643929	3645281
EcXA054	3440255	3445786
EcXA055	2724301	2729178

EXAMPLE 5

Identification of Individual Genes within an Operon Required for Proliferation

The following example illustrates a method for determining which gene in an operon is required for proliferation. The clone insert corresponding to Molecule No. EcXA004 possesses nucleic acid sequence homology to the *E. coli* genes *rspG* and *rspL*. This molecule corresponds to an operon containing two additional genes *fusA* and *tufA*. The *rspL* gene is the first gene in the operon. To determine which gene or genes in this operon are required for proliferation, each gene is selectively inactivated using homologous recombination. Gene *rspL* is the first gene to be inactivated.

Deletion inactivation of a chromosomal copy of a gene in *E. coli* can be accomplished by integrative gene replacement. The principle of this method (Hamilton, C. M., et al 1989. *J. Bacteriol.* 171: 4617-4622) is to construct a mutant allele of the targeted gene, introduce that allele into the chromosome using a conditional suicide vector, and then force the removal of the native wild type allele and vector sequences. This will replace the native gene with a desired mutation(s) but leave promoters, operators, etc. intact. Essentiality of a gene is determined either by deduction from genetic analysis or by conditional expression of a wild type copy of the targeted gene (trans complementation).

The first step is to generate a mutant *rspL* allele using PCR amplification. Two sets of PCR primers are chosen to produce a copy of *rspL* with a large central deletion to inactivate the gene. In order to eliminate polar effects, it is desirable to construct a mutant allele comprising an in-frame deletion of most or all of the coding region of the *rspL* gene. Each set of PCR primers is chosen such that a region flanking the gene to be amplified is sufficiently long to allow recombination (typically at least 500 nucleotides on each side of the deletion). The targeted deletion or mutation will be contained within this fragment. To facilitate cloning of the PCR product, the PCR primers may also contain restriction endonuclease sites found in the cloning region of a conditional knockout vector such as pK03 (Link, et al 1997 *J. Bacteriol.* 179 (20): 6228-6237). Suitable sites include NotI, SalI, BamHI and SmaI. The *rspL* gene fragments are produced using standard PCR conditions including, but not limited to, those outlined in the manufacturers directions for the

Hot Start Taq PCR kit (Qiagen, Inc., Valencia, CA). The PCR reactions will produce two fragments that can be fused together. Alternatively, crossover PCR can be used to generate a desired deletion in one step (Ho, S. N., et al 1989. *Gene* 77: 51-59, Horton, R. M., et al 1989. *Gene* 77: 61-68). The mutant allele thus produced is called a "null" allele because it cannot produce a functional gene product.

5 The mutant allele obtained from PCR amplification is cloned into the multiple cloning site of pK03. Directional cloning of the *rpsL* null allele is not necessary. The pK03 vector has a temperature-sensitive origin of replication derived from pSC101. Therefore, clones are propagated at the permissive temperature of 30°C. The vector also contains two selectable marker genes: one that confers resistance to chloramphenicol and another, the *Bacillus subtilis* *sacB* gene, that allows for counter-selection on sucrose containing growth medium. Clones that contain vector DNA with the null allele
10 inserted are confirmed by restriction endonuclease analysis and DNA sequence analysis of isolated plasmid DNA. The plasmid containing the *rpsL* null allele insert is known as a knockout plasmid.

Once the knockout plasmid has been constructed and its sequence verified, it is transformed into a Rec⁺ *E. coli* host cell. Transformation can be by any standard method such as electroporation. In some fraction of the transformed cells, plasmids will integrate into the *E. coli* chromosome by homologous recombination between the *rpsL* null allele in the
15 plasmid and the *rpsL* gene in the chromosome. Transformant colonies in which such an event has occurred are readily selected by growth at the non-permissive temperature of 43°C and in the presence of chloramphenicol. At this temperature, the plasmid will not replicate as an episome and will be lost from cells as they grow and divide. These cells are no longer resistant to chloramphenicol and will not grow when it is present. However, cells in which the knockout plasmid has integrated into the *E. coli* chromosome remain resistant to chloramphenicol and propagate.

20 Cells containing integrated knock-out plasmids are usually the result of a single crossover event that creates a tandem repeat of the mutant and native wild type alleles of *rpsL* separated by the vector sequences. A consequence of this is that *rpsL* will still be expressed in these cells. In order to determine if the gene is essential for growth, the wild type copy must be removed. This is accomplished by selecting for plasmid excision, a process in which homologous recombination between the two alleles results in looping out of the plasmid sequences. Cells that have undergone such an
25 excision event and have lost plasmid sequences including *sacB* gene are selected for by addition of sucrose to the medium. The *sacB* gene product converts sucrose to a toxic molecule. Thus counter selection with sucrose ensures that plasmid sequences are no longer present in the cell. Loss of plasmid sequences is further confirmed by testing for sensitivity to chloramphenicol (loss of the chloramphenicol resistance gene). The latter test is important because occasionally a mutation in the *sacB* gene can occur resulting in a loss of *sacB* function with no effect on plasmid replication (Link, et. al.,
30 1997 *J. Bacteriol.* 179 (20): 6228-6237). These artifact clones retain plasmid sequences and are therefore still resistant to chloramphenicol.

In the process of plasmid excision, one of the two *rpsL* alleles is lost from the chromosome along with the plasmid DNA. In general, it is equally likely that the null allele or the wild type allele will be lost. Therefore, if the *rpsL*

gene is not essential, half of the clones obtained in this experiment will have the wild type allele on the chromosome and half will have the null allele. However, if the *rpsL* gene is essential, cells containing the null allele will not be obtained as a single copy of the null allele would be lethal.

To determine the essentiality of *rpsL*, a statistically significant number of the resulting clones, at least 20, are analyzed by PCR amplification of the *rpsL* gene. Since the null allele is missing a significant portion of the *rpsL* gene, its PCR product is significantly shorter than that of the wild type gene and the two are readily distinguished by gel electrophoretic analysis. The PCR products may also be subjected to sequence determination for further confirmation by methods well known to those in the art.

The above experiment is generally adequate for determining the essentiality of a gene such as *rpsL*. However, it may be necessary or desirable to more directly confirm the essentiality of the gene. There are several methods by which this can be accomplished. In general, these involve three steps: 1) construction of an episome containing a wild type allele, 2) isolation of clones containing a single chromosomal copy of the mutant null allele as described above but in the presence of the episomal wild type allele, and then 3) determining if the cells survive when the expression of the episomal allele is shut off. In this case, the trans copy of wild type *rpsL* is made by PCR cloning of the entire coding region of *rpsL* and inserting it in the sense orientation downstream of an inducible promoter such as the *E. coli lac* promoter. Transcription of this allele of *rpsL* will be induced in the presence of IPTG which inactivates the *lac* repressor. Under IPTG induction *rpsL* protein will be expressed as long as the recombinant gene also possesses a ribosomal binding site, also known as a "Shine-Dalgarno Sequence". The trans copy of *rpsL* is cloned on a plasmid that is compatible with pSC101. Compatible vectors include p15A, pBR322, and the pUC plasmids, among others. Replication of the compatible plasmid will not be temperature-sensitive. The entire process of integrating the null allele of *rpsL* and subsequent plasmid excision is carried out in the presence of IPTG to ensure the expression of functional *rpsL* protein is maintained throughout. After the null *rpsL* allele is confirmed as integrated on the chromosome in place of the wild type *rpsL* allele, then IPTG is withdrawn and expression of functional *rpsL* protein shut off. If the *rpsL* gene is essential, cells will cease to proliferate under these conditions. However, if the *rpsL* gene is not essential, cells will continue to proliferate under these conditions. In this experiment, essentiality is determined by conditional expression of a wild type copy of the gene rather than inability to obtain the intended chromosomal disruption.

An advantage of this method over some other gene disruption techniques is that the targeted gene can be deleted or mutated without the introduction of large segments of foreign DNA. Therefore, polar effects on downstream genes are eliminated or minimized. There are methods described to introduce inducible promoters upstream of potential essential bacterial genes. However in such cases, polarity from multiple transcription start points can be a problem. One way of preventing this is to insert a gene disruption cassette that contains strong transcriptional terminators upstream of the integrated inducible promoter (Zhang, Y. and Cronan, J. E. 1996 *J. Bacteriol.* 178 (12): 3614-3620). The described techniques will all be familiar to one of ordinary skill in the art.

Following the analysis of the *rpsL* gene, the other genes of the operon are investigated to determine if they are required for proliferation.

EXAMPLE 6

Expression of the Proteins Encoded by Genes Identified as Required for *E. coli* Proliferation

5 The following is provided as one exemplary method to express the proliferation-required proteins encoded by the identified sequences described above. First, the initiation and termination codons for the gene are identified. If desired, methods for improving translation or expression of the protein are well known in the art. For example, if the nucleic acid encoding the polypeptide to be expressed lacks a methionine codon to serve as the initiation site, a strong Shine-Delgarno sequence, or a stop codon, these sequences can be added. Similarly, if the identified nucleic acid sequence lacks a transcription
10 termination signal, this sequence can be added to the construct by, for example, splicing out such a sequence from an appropriate donor sequence. In addition, the coding sequence may be operably linked to a strong promoter or an inducible promoter if desired. The identified nucleic acid sequence or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial expression vector or genome using oligonucleotide primers complementary to the identified nucleic acid sequence or portion thereof and containing restriction endonuclease sequences for *NcoI* incorporated into the 5' primer and
15 *BglII* at the 5' end of the corresponding 3'-primer, taking care to ensure that the identified nucleic acid sequence is positioned in frame with the termination signal. The purified fragment obtained from the resulting PCR reaction is digested with *NcoI* and *BglII*, purified and ligated to an expression vector.

The ligated product is transformed into DH5 α or some other *E. coli* strain suitable for the over expression of potential proteins. Transformation protocols are well known in the art. For example, transformation protocols are described in: **Current
20 Protocols in Molecular Biology**, Vol. 1, Unit 1.8, (Ausubel, et al., Eds.) John Wiley & Sons, Inc. (1997). Positive transformants are selected after growing the transformed cells on plates containing 50-100 μ g/ml Ampicillin (Sigma, St. Louis, Missouri). In one embodiment, the expressed protein is held in the cytoplasm of the host organism. In an alternate embodiment, the expressed protein is released into the culture medium. In still another alternative, the expressed protein can be sequestered in the periplasmic space and liberated therefrom using any one of a number of cell lysis techniques known in the art. For
25 example, the osmotic shock cell lysis method described in Chapter 16 of **Current Protocols in Molecular Biology**, Vol. 2, (Ausubel, et al., Eds.) John Wiley & Sons, Inc. (1997). Each of these procedures can be used to express a proliferation-required protein.

30 Expressed proteins, whether in the culture medium or liberated from the periplasmic space or the cytoplasm, are then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, standard chromatography, immunoprecipitation, immunochromatography, size exclusion chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein can be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment. The purity of the protein product

obtained can be assessed using techniques such as Coomassie or silver staining or using antibodies against the control protein. Coomassie and silver staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest can be generated using synthetic peptides using methods well known in the art. See, *Antibodies: A Laboratory Manual*, (Harlow and Lane, Eds.) Cold Spring Harbor Laboratory (1988). For example, 15-mer peptides having a sequence encoded by the appropriate identified gene sequence of interest or portion thereof can be chemically synthesized. The synthetic peptides are injected into mice to generate antibodies to the polypeptide encoded by the identified nucleic acid sequence of interest or portion thereof. Alternatively, samples of the protein expressed from the expression vectors discussed above can be purified and subjected to amino acid sequencing analysis to confirm the identity of the recombinantly expressed protein and subsequently used to raise antibodies. An Example describing in detail the generation of monoclonal and polyclonal antibodies appears in Example 7.

The protein encoded by the identified nucleic acid sequence of interest or portion thereof can be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques. These procedures are well known in the art.

In an alternative protein purification scheme, the identified nucleic acid sequence of interest or portion thereof can be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the identified nucleic acid sequence of interest or portion thereof is inserted in-frame with the gene encoding the other half of the chimera. The other half of the chimera can be maltose binding protein (MBP) or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to MBP or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites can be engineered between the MBP gene or the nickel binding polypeptide and the identified expected gene of interest, or portion thereof. Thus, the two polypeptides of the chimera can be separated from one another by protease digestion.

One useful expression vector for generating maltose binding protein fusion proteins is pMAL (New England Biolabs), which encodes the *malE* gene. In the pMal protein fusion system, the cloned gene is inserted into a pMal vector downstream from the *malE* gene. This results in the expression of an MBP-fusion protein. The fusion protein is purified by affinity chromatography. These techniques as described are well known to those skilled in the art of molecular biology.

EXAMPLE 7

Production of an Antibody to an isolated *E. coli* Protein

Substantially pure protein or polypeptide is isolated from the transformed cells as described in Example 6. The concentration of protein in the final preparation is adjusted, for example, by concentration on a 10,000 molecular weight cut off

AMICON filter device (Millipore, Bedford, MA), to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., *Nature* 256:495 (1975) or any of the well-known derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as described by Engvall, E., "Enzyme immunoassay ELISA and EMIT," *Meth. Enzymol.* 70:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. *Basic Methods in Molecular Biology* Elsevier, New York. Section 21-2.

Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogeneous epitopes of a single protein or a peptide can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than larger molecules and can require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. *J. Clin. Endocrinol. Metab.* 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: *Handbook of Experimental Immunology* D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: *Manual of Clinical Immunology*, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to

identify the presence of antigen in a biological sample. The antibodies can also be used in therapeutic compositions for killing bacterial cells expressing the protein.

EXAMPLE 8

Screening Chemical Libraries

A. Protein-Based Assays

Having isolated and expressed bacterial proteins shown to be required for bacterial proliferation, the present invention further contemplates the use of these expressed proteins in assays to screen libraries of compounds for potential drug candidates. The generation of chemical libraries is well known in the art. For example combinatorial chemistry can be used to generate a library of compounds to be screened in the assays described herein. A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical "building blocks" reagents. For example, a linear combinatorial chemical library such as a polypeptide library is formed by combining amino acids in every possible combination to yield peptides of a given length. Millions of chemical compounds theoretically can be synthesized through such combinatorial mixings of chemical building blocks. For example, one commentator observed that the systematic, combinatorial mixing of 100 interchangeable chemical building blocks results in the theoretical synthesis of 100 million tetrameric compounds or 10 billion pentameric compounds. (Gallop et al., "Applications of Combinatorial Technologies to Drug Discovery, Background and Peptide Combinatorial Libraries," *Journal of Medicinal Chemistry*, Vol. 37, No. 9, 1233-1250 (1994). Other chemical libraries known to those in the art may also be used, including natural product libraries.

Once generated, combinatorial libraries can be screened for compounds that possess desirable biological properties. For example, compounds which may be useful as drugs or to develop drugs would likely have the ability to bind to the target protein identified, expressed and purified as discussed above. Further, if the identified target protein is an enzyme, candidate compounds would likely interfere with the enzymatic properties of the target protein. Any enzyme can be a target protein. For example, the enzymatic function of a target protein can be to serve as a protease, nuclease, phosphatase, dehydrogenase, transporter protein, transcriptional enzyme, and any other type of enzyme known or unknown. Thus, the present invention contemplates using the protein products described above to screen combinatorial chemical libraries.

Those in the art will appreciate that a number of techniques exist for characterizing target proteins in order to identify molecules useful for the discovery and development of therapeutics. For example, some techniques involve the generation and use of small peptides to probe and analyze target proteins both biochemically and genetically in order to identify and develop drug leads. Such techniques include the methods described in PCT publications No. W09935494, W09819162, W09954728, the disclosures of which are incorporated herein by reference in their entireties.

In another example, the target protein is a serine protease and the substrate of the enzyme is known. The present example is directed towards the analysis of libraries of compounds to identify compounds that function as inhibitors of the target enzyme. First, a library of small molecules is generated using methods of combinatorial library formation well known in

the art. U.S. Patent NOs. 5,463,564 and 5,574, 656, to Agrafiotis, et al., entitled "System and Method of Automatically Generating Chemical Compound with Desired Properties," are two such teachings. Then the library compounds are screened to identify library compounds that possess desired structural and functional properties. U.S. Patent No. 5,684,711 also discusses a method for screening libraries.

5 To illustrate the screening process, the combined target and chemical compounds of the library are exposed to and permitted to interact with the purified enzyme. A labeled substrate is added to the incubation. The label on the substrate is such that a detectable signal is emitted from metabolized substrate molecules. The emission of this signal permits one to measure the effect of the combinatorial library compounds on the enzymatic activity of target enzymes. The characteristics of each library compound is encoded so that compounds demonstrating activity against the enzyme can be analyzed and features
10 common to the various compounds identified can be isolated and combined into future iterations of libraries.

Once a library of compounds is screened, subsequent libraries are generated using those chemical building blocks that possess the features shown in the first round of screen to have activity against the target enzyme. Using this method, subsequent iterations of candidate compounds will possess more and more of those structural and functional features required to inhibit the function of the target enzyme, until a group of enzyme inhibitors with high specificity for the enzyme can be found.
15 These compounds can then be further tested for their safety and efficacy as antibiotics for use in mammals.

It will be readily appreciated that this particular screening methodology is exemplary only. Other methods are well known to those skilled in the art. For example, a wide variety of screening techniques are known for a large number of naturally-occurring targets when the biochemical function of the target protein is known.

B. Cell Based Assays

20 Current cell-based assays used to identify or to characterize compounds for drug discovery and development frequently depend on detecting the ability of a test compound to inhibit the activity of a target molecule located within a cell or located on the surface of a cell. Most often such target molecules are proteins such as enzymes, receptors and the like. However, target molecules may also include other molecules such as DNAs, lipids, carbohydrates and RNAs including messenger RNAs, ribosomal RNAs, tRNAs and the like. A number of highly sensitive cell-based assay methods are
25 available to those of skill in the art to detect binding and interaction of test compounds with specific target molecules. However, these methods are generally not highly effective when the test compound binds to or otherwise interacts with its target molecule with moderate or low affinity. In addition, the target molecule may not be readily accessible to a test compound in solution, such as when the target molecule is located inside the cell or within a cellular compartment such as the periplasm of a bacterial cell. Thus, current cell-based assay methods are limited in that they are not effective in
30 identifying or characterizing compounds that interact with their targets with moderate to low affinity or compounds that interact with targets that are not readily accessible.

Cell-based assay methods of the present invention have substantial advantages over current cell-based assays practiced in the art. These advantages derive from the use of sensitized cells in which the level or activity of a

proliferation-required gene product (the target molecule) has been specifically reduced to the point where the presence or absence of its function becomes a rate-determining step for cellular proliferation. Bacterial, fungal, plant, or animal cells can all be used with the present method. Such sensitized cells become much more sensitive to compounds that are active against the affected target molecule. Thus, cell-based assays of the present invention are capable of detecting compounds exhibiting low or moderate potency against the target molecule of interest because such compounds are substantially more potent on sensitized cells than on non-sensitized cells. The affect may be such that a test compound may be two to several times more potent, at least 10 times more potent or even at least 100 times more potent when tested on the sensitized cells as compared to the non-sensitized cells.

Due in part to the increased appearance of antibiotic resistance in pathogenic microorganisms and to the significant side-effects associated with some currently used antibiotics, novel antibiotics acting at new targets are highly sought after in the art. Yet, another limitation in the current art related to cell-based assays is the problem of identifying hits against the same kinds of target molecules in the same limited set of biological pathways over and over again. This may occur when compounds acting at such new targets are discarded, ignored or fail to be detected because compounds acting at the "old" targets are encountered more frequently and are more potent than compounds acting at the new targets. As a result, the majority of antibiotics in use currently interact with a relatively small number of target molecules within an even more limited set of biological pathways.

The use of sensitized cells of the current invention provides a solution to the above problem in two ways. First, desired compounds acting at a target of interest, whether a new target or a previously known but poorly exploited target, can now be detected above the "noise" of compounds acting at the "old" targets due to the specific and substantial increase in potency of such desired compounds when tested on the sensitized cells of the current invention. Second, the methods used to sensitize cells to compounds acting at a target of interest may also sensitize these cells to compounds acting at other target molecules within the same biological pathway. For example, expression of an antisense molecule to a gene encoding a ribosomal protein is expected to sensitize the cell to compounds acting at that ribosomal protein and may also sensitize the cells to compounds acting at any of the ribosomal components (proteins or rRNA) or even to compounds acting at any target which is part of the protein synthesis pathway. Thus an important advantage of the present invention is the ability to reveal new targets and pathways that were previously not readily accessible to drug discovery methods.

Sensitized cells of the present invention are prepared by reducing the activity or level of a target molecule. The target molecule may be a gene product, such as an RNA or polypeptide produced from the proliferation-required nucleic acids described herein. Alternatively, the target may be a gene product such as an RNA or polypeptide which is produced form a sequence within the same operon as the proliferation-required nucleic acids described herein. In addition, the target may be an RNA or polypeptide in the same biological pathway as the proliferation-required nucleic acids described herein.

Such biological pathways include, but are not limited to, enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such the cell wall.

Current methods employed in the arts of medicinal and combinatorial chemistries are able to make use of structure-activity relationship information derived from testing compounds in various biological assays including direct binding assays and cell-based assays. Occasionally compounds are directly identified in such assays that are sufficiently potent to be developed as drugs. More often, initial hit compounds exhibit moderate or low potency. Once a hit compound is identified with low or moderate potency, directed libraries of compounds are synthesized and tested in order to identify more potent leads. Generally these directed libraries are combinatorial chemical libraries consisting of compounds with structures related to the hit compound but containing systematic variations including additions, subtractions and substitutions of various structural features. When tested for activity against the target molecule, structural features are identified that either alone or in combination with other features enhance or reduce activity. This information is used to design subsequent directed libraries containing compounds with enhanced activity against the target molecule. After one or several iterations of this process, compounds with substantially increased activity against the target molecule are identified and may be further developed as drugs. This process is facilitated by use of the sensitized cells of the present invention since compounds acting at the selected targets exhibit increased potency in such cell-based assays, thus; more compounds can now be characterized providing more useful information than would be obtained otherwise.

Thus, it is now possible using cell-based assays of the present invention to identify or characterize compounds that previously would not have been readily identified or characterized including compounds that act at targets that previously were not readily exploited using cell-based assays. The process of evolving potent drug leads from initial hit compounds is also substantially improved by the cell-based assays of the present invention because, for the same number of test compounds, more structure-function relationship information is likely to be revealed.

The method of sensitizing a cell entails selecting a suitable gene or operon. A suitable gene or operon is one whose expression is required for the proliferation of the cell to be sensitized. The next step is to introduce into the cells to be sensitized, an antisense RNA capable of hybridizing to the suitable gene or operon or to the RNA encoded by the suitable gene or operon. Introduction of the antisense RNA can be in the form of an expression vector in which antisense RNA is produced under the control of an inducible promoter. The amount of antisense RNA produced is limited by varying the inducer concentration to which the cell is exposed and thereby varying the activity of the promoter driving transcription of the antisense RNA. Thus, cells are sensitized by exposing them to an inducer concentration that results in a sub-lethal level of antisense RNA expression.

In one embodiment of the cell-based assays, the identified exogenous *E. coli* nucleotide sequences of the present invention are used to inhibit the production of a proliferation-required protein. Expression vectors producing antisense RNA against identified genes required for proliferation are used to limit the concentration of a proliferation-required protein without severely inhibiting growth. To achieve that goal, a growth inhibition dose curve of inducer is calculated by plotting

various doses of inducer against the corresponding growth inhibition caused by the antisense expression. From this curve, various percentages of antisense induced growth inhibition, from 1 to 100% can be determined. If the promoter contained in the expression vector contains a *lac* operator the transcription is regulated by *lac* repressor and expression from the promoter is inducible with IPTG. For example, the highest concentration of the inducer IPTG that does not reduce the growth rate (0% growth inhibition) can be predicted from the curve. Cellular proliferation can be monitored by growth medium turbidity via OD measurements. In another example, the concentration of inducer that reduces growth by 25% can be predicted from the curve. In still another example, a concentration of inducer that reduces growth by 50% can be calculated. Additional parameters such as colony forming units (cfu) can be used to measure cellular viability.

Cells to be assayed are exposed to the above-determined concentrations of inducer. The presence of the inducer at this sub-lethal concentration reduces the amount of the proliferation required gene product to the lowest amount in the cell that will support growth. Cells grown in the presence of this concentration of inducer are therefore specifically more sensitive to inhibitors of the proliferation-required protein or RNA of interest or to inhibitors of proteins or RNAs in the same biological pathway as the proliferation-required protein or RNA of interest but not to inhibitors of unrelated proteins or RNAs.

Cells pretreated with sub-inhibitory concentrations of inducer and thus containing a reduced amount of proliferation-required target gene product are then used to screen for compounds that reduce cell growth. The sub-lethal concentration of inducer may be any concentration consistent with the intended use of the assay to identify candidate compounds to which the cells are more sensitive. For example, the sub-lethal concentration of the inducer may be such that growth inhibition is at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60% at least about 75%, or more. Cells which are pre-sensitized using the preceding method are more sensitive to inhibitors of the target protein because these cells contain less target protein to inhibit than wild-type cells.

In another embodiment of the cell based assays of the present invention, the level or activity of a proliferation required gene product is reduced using a temperature sensitive ...mutation in the proliferation-required sequence and an antisense nucleic acid against the proliferation-required sequence. Growing the cells at an intermediate temperature between the permissive and restrictive temperatures of the temperature sensitive mutant where the mutation is in a proliferation-required gene produces cells with reduced activity of the proliferation-required gene product. The antisense RNA directed against the proliferation-required sequence further reduces the activity of the proliferation required gene product. Drugs that may not have been found using either the temperature sensitive mutation or the antisense nucleic acid alone may be identified by determining whether cells in which expression of the antisense nucleic acid has been induced and which are grown at a temperature between the permissive temperature and the restrictive temperature are substantially more sensitive to a test compound than cells in which expression of the antisense nucleic acid has not been induced and which are grown at a permissive temperature. Also drugs found previously from either the antisense nucleic acid alone or the

temperature sensitive mutation alone may have a different sensitivity profile when used in cells combining the two approaches, and that sensitivity profile may indicate a more specific action of the drug in inhibiting one or more activities of the gene product.

5 Temperature sensitive mutations may be located at different sites within the gene and correspond to different domains of the protein. For example, the *dnaB* gene of *Escherichia coli* encodes the replication fork DNA helicase. DnaB has several domains, including domains for oligomerization, ATP hydrolysis, DNA binding, interaction with primase, interaction with DnaC, and interaction with DnaA (Biswas, E.E. and Biswas, S.B. 1999. Mechanism and DnaB helicase of *Escherichia coli*: structural domains involved in ATP hydrolysis, DNA binding, and oligomerization. *Biochem.* 38:10919-10928; Hiasa, H. and Marians, K.J. 1999. Initiation of bidirectional replication at the chromosomal origin is directed by the interaction between helicase and primase. *J. Biol. Chem.* 274:27244-27248; San Martin, C., Rademacher, M., Wolpensinger, B., Engel, A., Miles, C.S., Dixon, N.E., and Carazo, J.M. 1998. Three-dimensional reconstructions from cryoelectron microscopy images reveal an intimate complex between helicase DnaB and its loading partner DnaC. *Structure* 6:501-9; Sutton, M.D., Carr, K.M., Vicente, M., and Kaguni, J.M. 1998. *Escherichia coli* DnaA protein. The N-terminal domain and loading of DnaB helicase at the *E. coli* chromosomal. *J. Biol. Chem.* 273:34255-62.), the disclosures of which are incorporated herein by reference in their entireties]. Temperature sensitive mutations in different domains of DnaB confer different phenotypes at the restrictive temperature, which include either an abrupt stop or slow stop in DNA replication with or without DNA breakdown (Wechsler, J.A. and Gross, J.D. 1971. *Escherichia coli* mutants temperature-sensitive for DNA synthesis. *Mol. Gen. Genetics* 113:273-284, the disclosure of which is incorporated herein by reference in its entirety) and termination of growth or cell death. Combining the use of temperature sensitive mutations in the *dnaB* gene that cause cell death at the restrictive temperature with an antisense to the *dnaB* gene could lead to the discovery of very specific and effective inhibitors of one or a subset of activities exhibited by DnaB.

20 When screening for antimicrobial agents against a gene product required for proliferation, growth inhibition of cells containing a limiting amount of that proliferation-required gene product can be assayed. Growth inhibition can be measured by directly comparing the amount of growth, measured by the optical density of the growth medium, between an experimental sample and a control sample. Alternative methods for assaying cell proliferation include measuring green fluorescent protein (GFP) reporter construct emissions, various enzymatic activity assays, and other methods well known in the art.

25 It will be appreciated that the above method may be performed in solid phase, liquid phase or a combination of the two. For example, cells grown on nutrient agar containing the inducer of the antisense construct may be exposed to compounds spotted onto the agar surface. A compound's effect may be judged from the diameter of the resulting killing zone, the area around the compound application point in which cells do not grow. Multiple compounds may be transferred to agar plates and simultaneously tested using automated and semi-automated equipment including but not restricted to

multi-channel pipettes (for example the Beckman Multimek) and multi-channel spotters (for example the Genomic Solutions Flexys). In this way multiple plates and thousands to millions of compounds may be tested per day.

The compounds may also be tested entirely in liquid phase using microtiter plates as described below. Liquid phase screening may be performed in microtiter plates containing 96, 384, 1536 or more wells per microtiter plate to screen multiple plates and thousands to millions of compounds per day. Automated and semi-automated equipment may be used for addition of reagents (for example cells and compounds) and determination of cell density.

EXAMPLE 9

The effectiveness of the above cell based assay was validated using constructs expressing antisense RNA to *E. coli* genes *rplL*, *rplJ*, and *rplW* encoding ribosomal proteins L7/L12, L10 and L23 respectively. These proteins are part of the protein synthesis apparatus of the cell and as such are required for proliferation. These constructs were used to test the effect of antisense expression on cell sensitivity to antibiotics known to bind to the ribosome and thereby inhibit protein synthesis. Constructs expressing antisense RNA to several other genes (*elaD*, *visC*, *yohH*, and *aptE/B*), the products of which are not involved in protein synthesis were used for comparison.

First expression vectors containing antisense constructs to either *rplW* or to *elaD* were introduced into separate *E. coli* cell populations. Vector introduction is a technique well known to those of ordinary skill in the art. The expression vectors of this example contain IPTG inducible promoters that drive the expression of the antisense RNA in the presence of the inducer. However, those skilled in the art will appreciate that other inducible promoters may also be used. Suitable expression vectors are also well known in the art. The *E. coli* antisense clones encoding ribosomal proteins L7/L12, L10 and L23 were used to test the effect of antisense expression on cell sensitivity to the antibiotics known to bind to these proteins. First, expression vectors containing antisense to either the genes encoding L7/L12 and L10 or L23 were introduced into separate *E. coli* cell populations.

The cell populations were exposed to a range of IPTG concentrations in liquid medium to obtain the growth inhibitory dose curve for each clone (Fig. 1). First, seed cultures were grown to a particular turbidity that is measured by the optical density (OD) of the growth solution. The OD of the solution is directly related to the number of bacterial cells contained therein. Subsequently, sixteen 200 μ l liquid medium cultures were grown in a 96 well microtiter plate at 37 C with a range of IPTG concentrations in duplicate two-fold serial dilutions from 1600 μ M to 12.5 μ M (final concentration). Additionally, control cells were grown in duplicate without IPTG. These cultures were started from equal amounts of cells derived from the same initial seed culture of a clone of interest. The cells were grown for up to 15 hours and the extent of growth was determined by measuring the optical density of the cultures at 600 nm. When the control culture reached mid-log phase the percent growth of the control for each of the IPTG containing cultures was plotted against the log concentrations of IPTG to produce a growth inhibitory dose response curve for the IPTG. The concentration of IPTG that inhibits cell growth to 50% (IC_{50}) as compared to the 0 mM IPTG control (0% growth inhibition) was then calculated from

the curve. Under these conditions, an amount of antisense RNA was produced that reduced the expression levels of *rplW* and *elaD* to a degree such that growth was inhibited by 50%.

Alternative methods of measuring growth are also contemplated. Examples of these methods include measurements of proteins, the expression of which is engineered into the cells being tested and can readily be measured. Examples of such proteins include green fluorescent protein (GFP) and various enzymes.

Cells were pretreated with the selected concentration of IPTG and then used to test the sensitivity of cell populations to tetracycline, erythromycin and other protein synthesis inhibitors. An example of a tetracycline dose response curve is shown in Figures 2A and 2B for the *rplW* and *elaD* genes, respectively. Cells were grown to log phase and then diluted into media alone or media containing IPTG at concentrations which give 20% and 50% growth inhibition as determined by IPTG dose response curves. After 2.5 hours, the cells were diluted to a final OD600 of 0.002 into 96 well plates containing (1) +/- IPTG at the same concentrations used for the 2.5 hour pre-incubation; and (2) serial two-fold dilutions of tetracycline such that the final concentrations of tetracycline range from 1 µg/ml to 15.6 ng/ml and 0 µg/ml. The 96 well plates were incubated at 37°C and the OD600 was read by a plate reader every 5 minutes for up to 15 hours. For each IPTG concentration and the no IPTG control, tetracycline dose response curves were determined when the control (absence of tetracycline) reached 0.1 OD600. To compare tetracycline sensitivity with and without IPTG, tetracycline IC50s were determined from the dose response curves (Figs. 2A-B). Cells with reduced levels of L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 2A) as compared to cells with reduced levels of *elaD* (Fig. 2B). Figure 3 shows a summary bar chart in which the ratios of tetracycline IC50s determined in the presence of IPTG which gives 50% growth inhibition versus tetracycline IC50s determined without IPTG (fold increase in tetracycline sensitivity) were plotted. Cells with reduced levels of either L7/L12 (genes *rplL*, *rplJ*) or L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 3). Cells expressing antisense to genes not known to be involved in protein synthesis (*atpB/E*, *visC*, *elaD*, *yohH*) did not show the same increased sensitivity to tetracycline, validating the specificity of this assay (Fig. 3).

In addition to the above, it has been observed in initial experiments that clones expressing antisense RNA to genes involved in protein synthesis (including genes encoding ribosomal proteins L7/L12 & L10, L7/L12 alone, L22, and L18, as well as genes encoding rRNA and Elongation Factor G) have increased sensitivity to the macrolide, erythromycin, whereas clones expressing antisense to the non-protein synthesis genes *elaD*, *atpB/E* and *visC* do not. Furthermore, the clone expressing antisense to *rplL* and *rplJ* does not show increased sensitivity to nalidixic acid and ofloxacin, antibiotics which do not inhibit protein synthesis.

The results with the ribosomal protein genes *rplL*, *rplJ*, and *rplW* as well as the initial results using various other antisense clones and antibiotics show that limiting the concentration of an antibiotic target makes cells more sensitive to the antimicrobial agents that specifically interact with that protein. The results also show that these cells are sensitized to antimicrobial agents that inhibit the overall function in which the protein target is involved but are not sensitized to antimicrobial agents that inhibit other functions.

The cell based assay described above may also be used to identify the biological pathway in which a proliferation-required nucleic acid or its gene product lies. In such methods, cells expressing a sub-lethal level of antisense to a target proliferation-required nucleic acid and control cells in which expression of the antisense has not been induced are contacted with a panel of antibiotics known to act in various pathways. If the antibiotic acts in the pathway in which the target proliferation-required nucleic acid or its gene product lies, cells in which expression of the antisense has been induced will be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced.

As a control, the results of the assay may be confirmed by contacting a panel of cells expressing antisense nucleic acids to many different proliferation-required genes including the target proliferation-required gene. If the antibiotic is acting specifically, heightened sensitivity to the antibiotic will be observed only in the cells expressing antisense to a target proliferation-required gene (or cells expressing antisense to other proliferation-required genes in the same pathway as the target proliferation-required gene) but will not be observed generally in all cells expressing antisense to proliferation-required genes.

Similarly, the above method may be used to determine the pathway on which a test antibiotic acts. A panel of cells, each of which expresses antisense to a proliferation-required nucleic acid in a known pathway, is contacted with a compound for which it is desired to determine the pathway on which it acts. The sensitivity of the panel of cells to the test compound is determined in cells in which expression of the antisense has been induced and in control cells in which expression of the antisense has not been induced. If the test antibiotic acts on the pathway on which an antisense nucleic acid acts, cells in which expression of the antisense has been induced will be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced. In addition, control cells in which expression of antisense to proliferation-required genes in other pathways has been induced will not exhibit heightened sensitivity to the antibiotic. In this way, the pathway on which the test antibiotic acts may be determined.

The Example below provides one method for performing such assays.

EXAMPLE 10

Identification of the Pathway in which a Proliferation-Required Gene Lies or the Pathway on which an Antibiotic Acts

A. Preparation of Bacterial Stocks for Assay

To provide a consistent source of cells to screen, frozen stocks of host bacteria containing the desired antisense construct are prepared using standard microbiological techniques. For example, a single clone of the organism can be isolated by streaking out a sample of the original stock onto an agar plate containing nutrients for cell growth and an antibiotic for which the antisense construct contains a gene which confers resistance. After overnight growth an isolated colony is picked from the plate with a sterile needle and transferred to an appropriate liquid growth media containing the antibiotic required for maintenance of the plasmid. The cells are incubated at 30°C to 37°C with vigorous shaking for 4 to

6 hours to yield a culture in exponential growth. Sterile glycerol is added to 15% (volume to volume) and 100 μ L to 500 μ L aliquots are distributed into sterile cryotubes, snap frozen in liquid nitrogen, and stored at -80°C for future assays.

B. Growth of Bacteria for Use in the Assay

5 A day prior to an assay, a stock vial is removed from the freezer, rapidly thawed (37°C water bath) and a loop of culture is streaked out on an agar plate containing nutrients for cell growth and an antibiotic to which the antisense construct confers resistance. After overnight growth at 37°C, ten randomly chosen, isolated colonies are transferred from the plate (sterile inoculum loop) to a sterile tube containing 5 mL of LB medium containing the antibiotic to which the antisense vector confers resistance. After vigorous mixing to form a homogeneous cell suspension, the optical density of the suspension is measured at 600 nm (OD600) and if necessary an aliquot of the suspension is diluted into a second tube of 5 mL, sterile, LB medium plus antibiotic to achieve an OD600 \leq 0.02 absorbance units. The culture is then incubated at 10 37° C for 1-2 hrs with shaking until the OD600 reaches OD 0.2 – 0.3. At this point the cells are ready to be used in the assay.

C. Selection of Media to be Used in Assay

15 Two fold dilution series of the inducer are generated in culture media containing the appropriate antibiotic for maintenance of the antisense construct. Several media are tested side by side and three to four wells are used to evaluate the effects of the inducer at each concentration in each media. For example, M9 minimal media, LB broth, TBD broth and Muller-Hinton media may be tested with the inducer IPTG at the following concentrations, 50 μ M, 100 μ M, 200 μ M, 400 μ M, 600 μ M, 800 μ M and 1000 μ M. Equal volumes of test media-inducer and cells are added to the wells of a 384 well microtiter plate and mixed. The cells are prepared as described above and diluted 1:100 in the appropriate media containing the test antibiotic immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several wells of each media that do not contain inducer, for example 0 M IPTG. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of inducer is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without inducer. The medium yielding greatest sensitivity to inducer is selected for use in the assays described below.

D. Measurement of Test Antibiotic Sensitivity in the Absence of Antisense Construct Induction

25 Two-fold dilution series of antibiotics of known mechanism of action are generated in the culture media selected for further assay development that has been supplemented with the antibiotic used to maintain the construct. A panel of test antibiotics known to act on different pathways is tested side by side with three to four wells being used to evaluate the effect of a test antibiotic on cell growth at each concentration. Equal volumes of test antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for assay development supplemented with the antibiotic required to maintain the antisense construct and are diluted 1:100 in identical media immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several

wells that contain the solvent used to dissolve the antibiotics but no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an IC₅₀ value for each antibiotic.

E. Measurement of Test Antibiotic Sensitivity in the Presence of Antisense Construct Inducer

The culture media selected for use in the assay is supplemented with inducer at concentrations shown to inhibit cell growth by 50 and 80% as described above and the antibiotic used to maintain the construct. Two fold dilution series of the panel of test antibiotics used above are generated in each of these media. Several antibiotics are tested side by side with three to four wells being used to evaluate the effects of an antibiotic on cell growth at each concentration, in each media. Equal volumes of test antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for use in the assay supplemented with the antibiotic required to maintain the antisense construct. The cells are diluted 1:100 into two 50 mL aliquots of identical media containing concentrations of inducer that have been shown to inhibit cell growth by 50% and 80 % respectively and incubated at 37°C with shaking for 2.5 hours. Immediately prior to addition to the microtiter plate wells, the cultures are adjusted to an appropriate OD₆₀₀ (typically 0.002) by dilution into warm (37°C) sterile media supplemented with identical concentrations of the inducer and antibiotic used to maintain the antisense construct. For a control, cells are also added to several wells that contain solvent used to dissolve test antibiotics but which contain no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an IC₅₀ value for each antibiotic.

F. Determining the Specificity of the Test Antibiotics

A comparison of the IC₅₀s generated by antibiotics of known mechanism of action under antisense induced and non-induced conditions allows the pathway in which a proliferation-required nucleic acid lies to be identified. If cells expressing an antisense nucleic acid against a proliferation-required gene are selectively sensitive to an antibiotic acting via a particular pathway, then the gene against which the antisense acts is involved in the pathway in which the antibiotic acts.

G. Identification of Pathway in which a Test Antibiotic Acts

As discussed above, the cell based assay may also be used to determine the pathway against which a test antibiotic acts. In such an analysis, the pathways against which each member of a panel of antisense nucleic acids acts are identified as described above. A panel of cells, each containing an inducible antisense vector against a gene in a known proliferation-required pathway, is contacted with a test antibiotic for which it is desired to determine the pathway

on which it acts under inducing an non-inducing conditions. If heightened sensitivity is observed in induced cells expressing antisense against a gene in a particular pathway but not in induced cells expressing antisense against genes in other pathways, then the test antibiotic acts against the pathway for which heightened sensitivity was observed.

One skilled in the art will appreciate that further optimization of the assay conditions, such as the concentration of inducer used to induce antisense expression and/or the growth conditions used for the assay (for example incubation temperature and media components) may further increase the selectivity and/or magnitude of the antibiotic sensitization exhibited.

The following example confirms the effectiveness of the methods described above.

EXAMPLE 11

Identification of the Pathway in which a Proliferation-Required Gene Lies

Antibiotics of various chemical classes and modes of action were purchased from Sigma Chemicals (St. Louis, MO). Stock solutions were prepared by dissolving each antibiotic in an appropriate aqueous solution based on information provided by the manufacturer. The final working solution of each antibiotic contained no more than 0.2% (w/v) of any organic solvent. To determine their potency against a bacterial strain engineered for expression of an antisense against a proliferation-required 50S ribosomal protein, each antibiotic was serially diluted two or three fold in growth medium supplemented with the appropriate antibiotic for maintenance of the anti-sense construct. At least ten dilutions were prepared for each antibiotic. 25 μ L aliquots of each dilution were transferred to discrete wells of a 384-well microplate (the assay plate) using a multi-channel pipette. Quadruplicate wells were used for each dilution of an antibiotic under each treatment condition (plus and minus inducer). Each assay plate contained twenty wells for cell growth controls (growth media replacing antibiotic), ten wells for each treatment (plus and minus inducer, in this example IPTG). Assay plates were usually divided into the two treatments: half the plate containing induced cells and an appropriate concentrations of inducer (in this example IPTG) to maintain the state of induction, the other half containing non-induced cells in the absence of IPTG.

Cells for the assay were prepared as follows. Bacterial cells containing a construct, from which expression of antisense nucleic acid against rplL and rplJ, which encode proliferation-required 50S ribosomal subunit proteins, is inducible in the presence of IPTG, were grown into exponential growth (OD_{600} 0.2 to 0.3) and then diluted 1:100 into fresh media containing either 400 μ M or 0 μ M inducer (IPTG). These cultures were incubated at 37° C for 2.5 hr. After a 2.5 hr incubation, induced and non-induced cells were respectively diluted into an assay medium at a final OD_{600} value of 0.0004. The medium contained an appropriate concentration of the antibiotic for the maintenance of the anti-sense construct. In addition, the medium used to dilute induced cells was supplemented with 800 μ M IPTG so that addition to the assay plate would result in a final IPTG concentration of 400 μ M. Induced and non-induced cell suspensions were dispensed (25 μ L/well) into the appropriate wells of the assay plate as discussed previously. The plate was then loaded into a plate reader, incubated at constant temperature, and cell growth was monitored in each well by the measurement of

light scattering at 595 nm. Growth was monitored every 5 minutes until the cell culture attained a stationary growth phase. For each concentration of antibiotic, a percentage inhibition of growth was calculated at the time point corresponding to mid-exponential growth for the associated control wells (no antibiotic, plus or minus IPTG). For each antibiotic and condition (plus or minus IPTG), a plot of percent inhibition versus log of antibiotic concentration was generated and the IC_{50} determined. A comparison of the IC_{50} for each antibiotic in the presence and absence of IPTG revealed whether induction of the antisense construct sensitized the cell to the mechanism of action exhibited by the antibiotic. Cells which exhibited a significant (standard statistical analysis) numerical decrease in the IC_{50} value in the presence of inducer were considered to have an increased sensitivity to the test antibiotic.

The results are provided in the table below, which lists the classes and names of the antibiotics used in the analysis, the targets of the antibiotics, the IC_{50} in the absence of IPTG, the IC_{50} in the presence of IPTG, the concentration units for the IC_{50} s, the fold increase in IC_{50} in the presence of IPTG, and whether increased sensitivity was observed in the presence of IPTG.

TABLE IV
Effect of Expression of Antisense RNA to rplL and rplJ on Antibiotic Sensitivity

ANTIBIOTIC CLASS /Names	TARGET	IC50 (-IPTG)	IC50 (+ IPTG)	Conc. Unit	Fold Increase in Sensitivity	Sensitivity Increased?
PROTEIN SYNTHESIS INHIBITOR ANTIBIOTICS						
AMINOGLYCOSIDES						
Gentamicin	30S ribosome function	2715	19.19	ng/ml	141	Yes
Streptomycin	30S ribosome function	11280	161	ng/ml	70	Yes
Spectinomycin	30S ribosome function	18050	< 156	ng/ml		Yes
Tobramycin	30S ribosome function	3594	70.58	ng/ml	51	Yes
MACROLIDES						
Erythromycin	50S ribosome function	7467	187	ng/ml	40	Yes
AROMATIC POYKETIDES						
Tetracycline	30S ribosome function	199.7	1.83	ng/ml	109	Yes
Minocycline	30S ribosome function	668.4	3.897	ng/ml	172	Yes
Doxycycline	30S ribosome function	413.1	27.81	ng/ml	15	Yes
OTHER PROTEIN SYNTHESIS INHIBITORS						
Fusidic acid	Elongation Factor G function	59990	641	ng/ml	94	Yes
Chloramphenicol	30S ribosome function	465.4	1.516	ng/ml	307	Yes
Lincomycin	50S ribosome function	47150	324.2	ng/ml	145	Yes
OTHER ANTIBIOTIC MECHANISMS						
B-LACTAMS						
Cefoxitin	Cell wall biosynthesis	2782	2484	ng/ml	1	No
Cefotaxime	Cell wall biosynthesis	24.3	24.16	ng/ml	1	No
DNA SYNTHESIS INHIBITORS						
Nalidixic acid	DNA Gyrase activity	6973	6025	ng/ml	1	No
Ofloxacin	DNA Gyrase activity	49.61	45.89	ng/ml	1	No
OTHER						
Bacitracin	Cell membrane function	4077	4677	mg/ml	1	No
Trimethoprim	Dihydrofolate Reductase activity	128.9	181.97	ng/ml	1	No
Vancomycin	Cell wall biosynthesis	145400	72550	ng/ml	2	No

The above results demonstrate that induction of an antisense RNA to genes encoding 50S ribosomal subunit proteins results in a selective and highly significant sensitization of cells to antibiotics that inhibit ribosomal function and protein synthesis. The above results further demonstrate that induction of an antisense construct to an essential gene sensitizes an organism to compounds that interfere with that gene products' biological role. This sensitization is restricted to compounds that interfere with pathways associated with the targeted gene and its product.

Assays utilizing antisense constructs to essential genes can be used to identify compounds that specifically interfere with the activity of multiple targets in a pathway. Such constructs can be used to simultaneously screen a sample against multiple targets in one pathway in one reaction (Combinatorial HTS).

Furthermore, as discussed above, panels of antisense construct containing cells may be used to characterize the point of intervention of any compound affecting an essential biological pathway including antibiotics with no known mechanism of action.

Another embodiment of the present invention is a method for determining the pathway against which a test antibiotic compound is active in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for determining which pathway a test antibiotic acts against except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using sublethal level of a known antibiotic which acts against the proliferation required gene product.

Interactions between drugs which affect the same biological pathway has been described in the literature. For example, Mecillinam (Amdinocillin) binds to and inactivates the penicillin binding protein 2 (PBP2, product of the *mrda* in *E. coli*). This antibiotic interacts with other antibiotics that inhibit PBP2 as well as antibiotics that inhibit other penicillin binding proteins such as PBP3 [(Gutmann, L., Vincent, S., Billot-Klein, D., Acar, J.F., Mrena, E., and Williamson, R. (1986) Involvement of penicillin-binding protein 2 with other penicillin-binding proteins in lysis of *Escherichia coli* by some beta-lactam antibiotics alone and in synergistic lytic effect of amdinocillin (mecillinam). *Antimicrobial Agents & Chemotherapy*, 30:906-912), the disclosure of which is incorporated herein by reference in its entirety]. Interactions between drugs could, therefore, involve two drugs that inhibit the same target protein or nucleic acid or inhibit different proteins or nucleic acids in the same pathway [(Fukuoka, T., Domon, H., Kakuta, M., Ishii, C., Hirasawa, A., Utsui, Y., Ohya, S., and Yasuda, H. (1997) Combination effect between panipenem and vancomycin on highly methicillin-resistant *Staphylococcus aureus*. *Japan. J. Antibio.* 50:411-419; Smith, C.E., Foleno, B.E., Barrett, J.F., and Frosc, M.B. (1997) Assessment of the synergistic interactions of levofloxacin and ampicillin against *Enterococcus faecium* by the checkerboard agar dilution and time-kill methods. *Diagnos. Microbiol. Infect. Disease* 27:85-92; den Hollander, J.G., Horrevorts, A.M., van Goor, M.L.,

Verbrugh, H.A., and Mouton, J.W. (1997) Synergism between tobramycin and ceftazidime against a resistant *Pseudomonas aeruginosa* strain, tested in an in vitro pharmacokinetic model. *Antimicrobial Agents & Chemotherapy*. 41:95-110), the disclosure of all of which are incorporated herein by reference in their entireties].

Two drugs may interact even though they inhibit different targets. For example, the proton pump inhibitor, Omeprazole, and the antibiotic, Amoxycillin, two synergistic compounds acting together, can cure *Helicobacter pylori* infection [(Gabryelewicz, A., Laszewicz, W., Dzieńiszewski, J., Ciok, J., Marlicz, K., Bielecki, D., Popiela, T., Legutko, J., Knapik, Z., Poniewierka, E. (1997) Multicenter evaluation of dual-therapy (omeprazol and amoxycillin) for *Helicobacter pylori*-associated duodenal and gastric ulcer (two years of the observation). *J. Physiol. Pharmacol.* 48 Suppl 4:93-105), the disclosure of which is incorporated herein by reference in its entirety].

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

Cells are contacted with a combination of each member of a panel of known antibiotics at a sublethal level and varying concentrations of the test antibiotic. As a control, the cells are contacted with varying concentrations of the test antibiotic alone. The IC_{50} of the test antibiotic in the presence and absence of the known antibiotic is determined. If the IC_{50} s in the presence and absence of the known drug are substantially similar, then the test drug and the known drug act on different pathways. If the IC_{50} s are substantially different, then the test drug and the known drug act on the same pathway.

Another embodiment of the present invention is a method for identifying a candidate compound for use as an antibiotic in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for identifying candidate compounds for use as antibiotics except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using a sublethal level of a known antibiotic which acts against the proliferation required gene product.

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

In order to characterize test compounds of interest, cells are contacted with a panel of known antibiotics at a sublethal level and one or more concentrations of the test compound. As a control, the cells are contacted with the same concentrations of the test compound alone. The IC_{50} of the test compound in the presence and absence of the known antibiotic is determined. If the IC_{50} of the test compound is substantially different in the presence and absence of the known drug then the test compound is a good candidate for use as an antibiotic. As discussed above, once a candidate compound is identified using the above methods its structure may be optimized using standard techniques such as combinatorial chemistry.

Representative known antibiotics which may be used in each of the above methods are provided in the table below. However, it will be appreciated that other antibiotics may also be used.

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Inhibitors of Transcription		
Rifamycin, 1959 Rifampicin	Inhibits initiation of transcription/ β -subunit RNA polymerase, <i>rpoB</i>	<i>rpoB</i> , <i>crp</i> , <i>cyaA</i>
Rifabutin Rifaximin		
Streptolydigin	Accelerates transcription chain termination/ β -subunit RNA polymerase	<i>rpoB</i>
Streptovaricin	an acyclic ansamycin, inhibits RNA polymerase	<i>rpoB</i>
Actinomycin D + EDTA	Intercalates between 2 successive G-C pairs, <i>rpoB</i> , inhibits RNA synthesis	<i>pldA</i>
Inhibitors of Nucleic Acid Metabolism		
Quinolones, 1962 Nalidixic acid	subunit gyrase and/or topoisomerase IV, <i>gyrA</i>	<i>gyrAorB</i> , <i>icd</i> , <i>sloB</i>
Oxolinic acid		
Fluoroquinolones Ciprofloxacin, 1983 Norfloxacin	subunit gyrase, <i>gyrA</i> and/or topoisomerase IV (probable target in Staph)	<i>gyrA</i> <i>norA</i> (efflux in Staph) <i>hipQ</i>
Coumerins Novobiocin	Inhibits ATPase activity of β -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>cysB</i> , <i>cysE</i> , <i>nov</i> , <i>ompA</i>
Coumermycin	Inhibits ATPase activity of β -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>hisW</i>
Albicidin	DNA synthesis	<i>tsx</i> (nucleoside channel)
Metronidazole	Causes single-strand breaks in DNA	<i>nar</i>
Inhibitors of Metabolic Pathways		
Sulfonamides, 1932 Sulfanilamide	blocks synthesis of dihydrofolate, dihydro- pteroate synthesis, <i>folP</i>	<i>folP</i> , <i>gpt</i> , <i>pabA</i> , <i>pabB</i> , <i>pabC</i>
Trimethoprim, 1962	Inhibits dihydrofolate reductase, <i>folA</i>	<i>folA</i> , <i>thyA</i>
Showdomycin	Nucleoside analogue capable of alkylating	<i>nupC</i> , <i>pnp</i>

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Thiolactomycin	sulfhydryl groups, inhibitor of thymidylate synthetase type II fatty acid synthase inhibitor	<i>emrB</i> <i>fadB</i> , <i>emrB</i> due to gene dosage <i>guaA,B</i>
Psicofuranine	Adenosine glycoside antibiotic, target is GMP synthetase	<i>fabI (envM)</i> <i>fabI (envM)</i>
Triclosan	Inhibits fatty acid synthesis	
Diazaborines Isoniazid, Ethionamide	heterocyclic, contains boron, inhibit fatty acid synthesis, enoyl-ACP reductase, <i>fabI</i>	
Inhibitors of Translation		
Phenylpropanoids Chloramphenicol, 1947	Binds to ribosomal peptidyl transfer center preventing peptide translocation/ binds to S6, L3, L6, L14, L16, L25, L26, L27, but preferentially to L16	<i>rrn</i> , <i>cmlA</i> , <i>marA</i> , <i>ompF</i> , <i>ompR</i>
Tetracyclines, 1948, type II polyketides Minocycline Doxycycline	Binding to 30S ribosomal subunit, "A" site on 30S subunit, blocks peptide elongation, strongest binding to S7	<i>clmA (cmr)</i> , <i>mar</i> , <i>ompF</i>
Macrolides (type I polyketides) Erythromycin, 1950 Carbamycin, Spiramycin	Binding to 50 S ribosomal subunit, 23S rRNA, blocks peptide translocation, L15, L4, L12	<i>rm</i> , <i>rplC</i> , <i>rplD</i> , <i>rplV</i> , <i>mac</i>
etc		
Aminoglycosides Streptomycin, 1944 Neomycin	Irreversible binding to 30S ribosomal subunit, prevents translation or causes mistranslation of mRNA/16S rRNA	<i>rpsL</i> , <i>strC,M</i> , <i>ubiF</i> <i>atpA-E</i> , <i>ecfB</i> , <i>hemAC,D,E,G</i> , <i>topA</i> , <i>rpsC,D,E</i> , <i>rm</i> , <i>spcB</i> <i>atpA-atpE</i> , <i>cpxA</i> , <i>ecfB</i> , <i>hemA,B,L</i> , <i>topA</i> <i>ksgA,B,C,D</i> , <i>rplB,K</i> , <i>rpsL,N,M,R</i> <i>rplF</i> , <i>ubiF</i> <i>cpxA</i> <i>rpsL</i>
Spectinomycin Kanamycin		
Kasugamycin		
Gentamicin, 1963 Amikacin Paromycin		
Lincosamides Lincomycin, 1955 Clindamycin	Binding to 50 S ribosomal subunit, blocks peptide translocation	<i>linB</i> , <i>rplN,O</i> , <i>rpsG</i>
Streptogramins Virginiamycin, 1955 Pristinamycin	2 components, Streptogramins A&B, bind to the 50S ribosomal subunit blocking peptide translocation and peptide bond formation	
Synercid: quinupristin /dalfopristin		
Fusidanes Fusidic Acid	Inhibition of elongation factor G (EF-G) prevents peptide translocation	<i>fusA</i>
Kirromycin (Mocimycin)	Inhibition of elongation factor TU (EF-Tu), prevents peptide bond formation	<i>tufA,B</i>

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Pulvomycin	Binds to and inhibits EF-TU	
Thiopeptin	Sulfur-containing antibiotic, inhibits protein synthesis, EF-G	<i>rpIE</i>
Tiamulin	Inhibits protein synthesis	<i>rpIC, rpID</i>
Negamycin	Inhibits termination process of protein synthesis	<i>prfB</i>
Oxazolidinones Linezolid Isoniazid	23S rRNA	
Nitrofurantoin	Inhibits protein synthesis, nitroreductases convert nitrofurantoin to highly reactive electrophilic intermediates which attack bacterial ribosomal proteins non-specifically	<i>pdx</i> <i>nfnA, B</i>
Pseudomonic Acids Mupirocin (Bactroban)	Inhibition of isoleucyl tRNA synthetase-used for Staph, topical cream, nasal spray	<i>ileS</i>
Indolmycin	Inhibits tryptophanyl-tRNA synthetase	<i>trpS</i>
Viomycin		<i>rrmA</i> (23S rRNA methyltransferase; mutant has slow growth rate, slow chain elongation rate, and viomycin resistance)
Thiopeptides	Binds to L11-23S RNA complex	
Thiostrepton	Inhibits GTP hydrolysis by EF-G	
Micrococcin	Stimulates GTP hydrolysis by EF-G	
Inhibitors of Cell Walls/Membranes		
β-lactams		
Penicillin, 1929 Ampicillin	Inhibition of one or more cell wall transpeptidases, endopeptidases, and glycosidases (PBPs), of the 12 PBPs only 2 are essential: <i>mrdA</i> (PBP2) and <i>ftsI</i> (<i>pbpB</i> , PBP3)	<i>ampC, ampD, ampE, envZ, galU, hipA, hipQ, ompC, ompF, ompR, ptsI, rfa, tolD, tolE</i>
Methicillin, 1960		
Cephalosporins, 1962		<i>tonB</i>
Mecillinam (amdinocillin)	Binds to and inactivates PBP2 (<i>mrdA</i>) Inactivates PBP3 (<i>ftsI</i>)	<i>alaS, argS, crp, cyaA, envB, mrdA, B, mreB, C, D</i>
Aztreonam (Furazlocillin)		
Bacilysin, Tetaine	Dipeptide, inhib glucosamine synthase	<i>dppA</i>
Glycopeptides Vancomycin, 1955	Inhib G+ cell wall syn, binds to terminal D-ala-D-ala of pentapeptide,	
Polypeptides Bacitracin	Prevents dephosphorylation and regeneration of lipid carrier	<i>rfa</i>
Cyclic lipopeptide Daptomycin, 1980	Disrupts multiple aspects of membrane	

	function, including peptidoglycan synthesis, lipoteichoic acid synthesis, and the bacterial membrane potential	
Cyclic polypeptides Polymixin, 1939	Surfactant action disrupts cell membrane lipids, binds lipid A moiety of LPS	<i>pmrA</i>
Fosfomycin, 1969	Analogue of P-enolpyruvate, inhibits 1 st step in peptidoglycan synthesis - UDP-N-acetylglucosamine enolpyruvyl transferase, <i>murA</i> . Also acts as Immunosuppressant	<i>murA, crp, cyaA glpT, hipA, ptsI, uhpT</i>
Cycloserine	Prevents formation of D-alanine dimer, inhibits D-alanine ligase, <i>ddlA,B</i>	<i>hipA, cycA</i>
Alafosfalin	phosphonodipeptide, cell wall synthesis inhibitor, potentiator of β -lactams	<i>pepA, tpp</i>
Inhibitors of Protein Processing/Transport		
Globomycin	Inhibits signal peptidase II (cleaves polipoproteins subsequent to lipid modification, <i>lspA</i>)	<i>lpp, dnaE</i>

EXAMPLE 12

Transfer of Exogenous Nucleic Acid Sequences to other Bacterial Species Using the *E. coli* Expression Vectors or Expression Vectors Functional in Bacterial Species other than *E. coli*.

5 The above methods were validated using antisense nucleic acids which inhibit the growth of *E. coli* which were identified using methods similar to those described above. Expression vectors which inhibited growth of *E. coli* upon induction of antisense RNA expression with IPTG were transformed directly into *Enterobacter cloacae*, *Klebsiella pneumoniae* or *Salmonella typhimurium*. The transformed cells were then assayed for growth inhibition according to the method of Example 1. After growth in liquid culture, cells were plated at various serial dilutions and a score determined by calculating the log difference in growth for INDUCED vs. UNINDUCED antisense RNA expression as determined by the maximum 10 fold dilution at which a colony was observed. The results of these experiments are listed below in Table VI. If there was no effect of antisense RNA expression in an organism, the clone is minus in Table VI. In contrast, a positive in Table VI means that at least 10 fold more cells were required to observe a colony on the induced plate than on the non-induced plate under the conditions used and in that organism.

15 Sixteen of the constructs were found to inhibit growth in all the organisms tested upon induction of antisense RNA expression with IPTG. Those skilled in the art will appreciate that a negative result in a heterologous organism does not mean that that organism is missing that gene nor does it mean that the gene is unessential. However, a positive result means that the heterologous organism contains a homologous gene which is required for proliferation of that organism. The homologous gene may be obtained using the methods described herein. Those cells that are inhibited by antisense may be used in cell based assays as described herein for the identification and characterization of compounds in order to

develop antibiotics effective in these organisms. Those skilled in the art will appreciate that an antisense molecule which works in the organism from which it was obtained will not always work in a heterologous organism.

TABLE VI

Sensitivity of Other Microorganisms to Antisense Nucleic Acids That Inhibit Proliferation in *E. coli*

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA001	+	+	.
EcXA004	.	.	.
EcXA005	+	+	+
EcXA006	.	.	.
EcXA007	.	+	.
EcXA008	+	.	+
EcXA010	+	+	+
EcXA011	.	+	.
EcXA012	.	+	.
EcXA013	+	+	+
EcXA014	+	+	.
EcXA015	.	+	+
EcXA016	+	+	+
EcXA017	+	+	+
EcXA018	+	+	+
EcXA019	+	+	+
EcXA020	+	+	+
EcXA021	+	+	+
EcXA023	+	+	+
EcXA024	+	.	+
EcXA025	.	.	.
EcXA026	+	+	.
EcXA027	+	+	+
EcXA028	+	.	.
EcXA029	.	.	.

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA030	+	+	+
EcXA031	+	.	.
EcXA032	+	.	.
EcXA033	+	+	+
EcXA034	+	+	+
EcXA035	.	.	.
EcXA036	+	.	+
EcXA037	.	+	.
EcXA038	+	+	.
EcXA039	+	.	.
EcXA041	+	+	+
EcXA042	.	+	+
EcXA044	.	.	.
EcXA045	.	+	.
EcXA046	.	.	.
EcXA047	+	+	.
EcXA048	.	.	.
EcXA049	+	.	.
EcXA050	.	.	.
EcXA051	+	.	.
EcXA052	+	.	.
EcXA053	+	+	+
EcXA054	.	.	+
EcXA055	+	.	.

EXAMPLE 13

Use of Identified Exogenous Nucleic Acid Sequences as Probes

5

The identified sequence of the present invention can be used as probes to obtain the sequence of additional genes of interest from a second organism. For example, probes to potential bacterial target proteins may be hybridized to nucleic acids from other organisms including other bacteria and higher organisms, to identify homologous sequences. Such

hybridization might indicate that the protein encoded by the gene to which the probe corresponds is found in humans and therefore not necessarily a good drug target. Alternatively, the gene can be conserved only in bacteria and therefore would be a good drug target for a broad spectrum antibiotic or antimicrobial.

Probes derived from the identified nucleic acid sequences of interest or portions thereof can be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe can be single stranded or double stranded and can be made using techniques known in the art, including *in vitro* transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it can be denatured prior to contacting the probe. In some applications, the nucleic acid sample can be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample can comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe can be cloned into vectors such as expression vectors, sequencing vectors, or *in vitro* transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques can be used to isolate, purify and clone sequences from a genomic library, made from a variety of bacterial species, which are capable of hybridizing to probes made from the sequences identified in Examples 5 and 6.

EXAMPLE 14

Preparation of PCR Primers and Amplification of DNA

The identified *E. coli* genes corresponding directly to or located within the operon of nucleic acid sequences required for proliferation or portions thereof can be used to prepare PCR primers for a variety of applications, including the identification or isolation of homologous sequences from other species, for example *S. typhimurium*, *E. cloacae*, and *Klebsiella pneumoniae*, which contain part or all of the homologous genes. Because homologous genes are related but not identical in sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on conserved sequence regions, either known or suspected, such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers are at least 10 bases, and preferably at least 20 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers can be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in *Methods in Molecular Biology* 67: Humana Press, Totowa 1997. When the entire coding sequence of the target gene is known, the 5' and 3' regions of the target gene

can be used as the sequence source for PCR probe generation. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

EXAMPLE 15

Inverse PCR

The technique of inverse polymerase chain reaction can be used to extend the known nucleic acid sequence identified in Examples 5 and 6. The inverse PCR reaction is described generally by Ochman et al., in Ch. 10 of **PCR Technology: Principles and Applications for DNA Amplification**, (Henry A. Erlich, Ed.) W.H. Freeman and Co. (1992). Traditional PCR requires two primers that are used to prime the synthesis of complementary strands of DNA. In inverse PCR, only a core sequence need be known.

Using the sequences identified as relevant from the techniques taught in Examples 5 and 6 and applied to other species of bacteria, a subset of exogenous nucleic sequences are identified that correspond to genes or operons that are required for bacterial proliferation. In species for which a genome sequence is not known, the technique of inverse PCR provides a method for obtaining the gene in order to determine the sequence or to place the probe sequences in full context to the target sequence to which the identified exogenous nucleic acid sequence binds.

To practice this technique, the genome of the target organism is digested with an appropriate restriction enzyme so as to create fragments of nucleic acid that contain the identified sequence as well as unknown sequences that flank the identified sequence. These fragments are then circularized and become the template for the PCR reaction. PCR primers are designed in accordance with the teachings of Example 15 and directed to the ends of the identified sequence are synthesized. The primers direct nucleic acid synthesis away from the known sequence and toward the unknown sequence contained within the circularized template. After the PCR reaction is complete, the resulting PCR products can be sequenced so as to extend the sequence of the identified gene past the core sequence of the identified exogenous nucleic acid sequence identified. In this manner, the full sequence of each novel gene can be identified. Additionally the sequences of adjacent coding and noncoding regions can be identified.

EXAMPLE 16

Identification of Genes Required for *Staphylococcus aureus* Proliferation

Genes required for proliferation in *Staphylococcus aureus* are identified according to the methods described above.

EXAMPLE 17

Identification of Genes Required for *Neisseria gonorrhoeae* Proliferation

Genes required for proliferation in *Neisseria gonorrhoeae* are identified according to the methods described above.

EXAMPLE 18**Identification of Genes Required for *Pseudomonas aeruginosa* Proliferation**

Genes required for proliferation in *Pseudomonas aeruginosa* are identified according to the methods described above.

EXAMPLE 19**Identification of Genes Required for *Enterococcus faecalis* Proliferation**

Genes required for proliferation in *Enterococcus faecalis* are identified according to the methods described above.

EXAMPLE 20**Identification of Genes Required for *Haemophilus influenzae* Proliferation**

Genes required for proliferation in *Haemophilus influenzae* are identified according to the methods described above.

EXAMPLE 21**Identification of Genes Required for *Salmonella typhimurium* Proliferation**

Genes required for proliferation in *Salmonella typhimurium* are identified according to the methods described above.

EXAMPLE 22**Identification of Genes Required for *Helicobacter pylori* Proliferation**

Genes required for proliferation in *Helicobacter pylori* are identified according to the methods described above.

EXAMPLE 23**Identification of Genes Required for *Mycoplasma pneumoniae* Proliferation**

Genes required for proliferation in *Mycoplasma pneumoniae* are identified according to the methods described above.

EXAMPLE 24**Identification of Genes Required for *Plasmodium ovale* Proliferation**

Genes required for proliferation in *Plasmodium ovale* are identified according to the methods described above.

EXAMPLE 25**Identification of Genes Required for *Saccharomyces cerevisiae* Proliferation**

Genes required for proliferation in *Saccharomyces cerevisiae* are identified according to the methods described above.

EXAMPLE 26**Identification of Genes Required for *Entamoeba histolytica* Proliferation**

Genes required for proliferation in *Entamoeba histolytica* are identified according to the methods described above.

EXAMPLE 27**Identification of Genes Required for *Candida albicans* Proliferation**

Genes required for proliferation in *Candida albicans* are identified according to the methods described above.

EXAMPLE 28Identification of Genes Required for *Klebsiella pneumoniae* Proliferation

Genes required for proliferation in *Klebsiella pneumoniae* are identified according to the methods described above.

EXAMPLE 29Identification of Genes Required for *Salmonella typhi* Proliferation

Genes required for proliferation in *Salmonella typhi* are identified according to the methods described above.

EXAMPLE 30Identification of Genes Required for *Salmonella paratyphi* Proliferation

Genes required for proliferation in *Salmonella paratyphi* are identified according to the methods described above.

EXAMPLE 31Identification of Genes Required for *Salmonella choleraesuis* Proliferation

Genes required for proliferation in *Salmonella choleraesuis* are identified according to the methods described above.

EXAMPLE 32Identification of Genes Required for *Staphylococcus epidermis* Proliferation

Genes required for proliferation in *Staphylococcus epidermis* are identified according to the methods described above.

EXAMPLE 33Identification of Genes Required for *Mycobacterium tuberculosis* Proliferation

Genes required for proliferation in *Mycobacterium tuberculosis* are identified according to the methods described above.

EXAMPLE 34Identification of Genes Required for *Mycobacterium leprae* Proliferation

Genes required for proliferation in *Mycobacterium leprae* are identified according to the methods described above.

EXAMPLE 35Identification of Genes Required for *Treponema pallidum* Proliferation

Genes required for proliferation in *Treponema pallidum* are identified according to the methods described above.

EXAMPLE 36Identification of Genes Required for *Bacillus anthracis* Proliferation

Genes required for proliferation in *Bacillus anthracis* are identified according to the methods described above.

EXAMPLE 37Identification of Genes Required for *Yersinia pestis* Proliferation

Genes required for proliferation in *Yersinia pestis* are identified according to the methods described above.

EXAMPLE 38**Identification of Genes Required for *Clostridium botulinum* Proliferation**

Genes required for proliferation in *Clostridium botulinum* are identified according to the methods described above.

EXAMPLE 39**Identification of Genes Required for *Campylobacter jejuni* Proliferation**

Genes required for proliferation in *Campylobacter jejuni* are identified according to the methods described above.

EXAMPLE 40**Identification of Genes Required for *Chlamydia trachomatis* Proliferation**

Genes required for proliferation in *Chlamydia trachomatis* are identified according to the methods described above.

Use of Isolated Exogenous Nucleic Acid Fragments as Antisense Antibiotics

In addition to using the identified sequences to enable screening of molecule libraries to identify compounds useful to identify antibiotics, the sequences themselves can be used as therapeutic agents. Specifically, the identified exogenous sequences in an antisense orientation can be provided to an individual to inhibit the translation of a bacterial target gene.

Generation of Antisense Therapeutics from Identified Exogenous Sequences

The sequences of the present invention can be used as antisense therapeutics for the treatment of bacterial infections or simply for inhibition of bacterial growth *in vitro* or *in vivo*. The therapy exploits the biological process in cells where genes are transcribed into messenger RNA (mRNA) that is then translated into proteins. Antisense RNA technology contemplates the use of antisense oligonucleotides directed against a target gene that will bind to its target and decrease or inhibit the translation of the target mRNA. In one embodiment, antisense oligonucleotides can be used to treat and control a bacterial infection of a cell culture containing a population of desired cells contaminated with bacteria. In another embodiment, the antisense oligonucleotides can be used to treat an organism with a bacterial infection.

Antisense oligonucleotides can be synthesized from any of the sequences of the present invention using methods well known in the art. In a preferred embodiment, antisense oligonucleotides are synthesized using artificial means. Uhlmann & Peymann, Chemical Rev. 90:543-584 (1990) review antisense oligonucleotide technology in detail. Modified or unmodified antisense oligonucleotides can be used as therapeutic agents. Modified antisense oligonucleotides are preferred since it is well known that antisense oligonucleotides are extremely unstable. Modification of the phosphate backbones of the antisense oligonucleotides can be achieved by substituting the internucleotide phosphate residues with methylphosphonates, phosphorothioates, phosphoramidates, and phosphate esters. Nonphosphate internucleotide analogs such as siloxane bridges, carbonate bridges, thioester bridges, as well as many others known in the art. The preparation of certain antisense oligonucleotides with modified internucleotide linkages is described in U.S. Patent No. 5,142,047, hereby incorporated by reference.

Modifications to the nucleoside units of the antisense oligonucleotides are also contemplated. These modifications can increase the half-life and increase cellular rates of uptake for the oligonucleotides *in vivo*. For example,

α -anomeric nucleotide units and modified bases such as 1,2-dideoxy-d-ribofuranose, 1,2-dideoxy-1-phenyltribofuranose, and *N*, *N*-ethano-5-methyl-cytosine are contemplated for use in the present invention.

An additional form of modified antisense molecules is found in peptide nucleic acids. Peptide nucleic acids (PNA) have been developed to hybridize to single and double stranded nucleic acids. PNA are nucleic acid analogs in which the entire deoxyribose-phosphate backbone has been exchanged with a chemically completely different, but structurally homologous, polyamide (peptide) backbone containing 2-aminoethyl glycine units. Unlike DNA, which is highly negatively charged, the PNA backbone is neutral. Therefore, there is much less repulsive energy between complementary strands in a PNA-DNA hybrid than in the comparable DNA-DNA hybrid, and consequently they are much more stable. PNA can hybridize to DNA in either a Watson/Crick or Hoogsteen fashion (Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:2637-2641, 1995; Egholm, *Nature* 365:566-568, 1993; Nielsen et al., *Science* 254:1497-1500, 1991; Dueholm et al., *New J. Chem.* 21:19-31, 1997).

Molecules called PNA "clamps" have been synthesized which have two identical PNA sequences joined by a flexible hairpin linker containing three 8-amino-3,6-dioxaoctanoic acid units. When a PNA clamp is mixed with a complementary homopurine or homopyrimidine DNA target sequence, a PNA-DNA-PNA triplex hybrid can form which has been shown to be extremely stable (Bentin et al., *Biochemistry* 35:8863-8869, 1996; Egholm et al., *Nucleic Acids Res.* 23:217-222, 1995; Griffith et al., *J. Am. Chem. Soc.* 117:831-832, 1995).

The sequence-specific and high affinity duplex and triplex binding of PNA have been extensively described (Nielsen et al., *Science* 254:1497-1500, 1991; Egholm et al., *J. Am. Chem. Soc.* 114:9677-9678, 1992; Egholm et al., *Nature* 365:566-568, 1993; Almarsson et al., *Proc. Natl. Acad. Sci. U.S.A.* 90:9542-9546, 1993; Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:2637-2641, 1995). They have also been shown to be resistant to nuclease and protease digestion (Demidov et al., *Biochem. Pharm.* 48:1010-1313, 1994). PNA has been used to inhibit gene expression (Hanvey et al., *Science* 258:1481-1485, 1992; Nielsen et al., *Nucl. Acids. Res.*, 21:197-200, 1993; Nielsen et al., *Gene* 149:139-145, 1994; Good & Nielsen, *Science*, 95: 2073-2076, 1998; all of which are hereby incorporated by reference), to block restriction enzyme activity (Nielsen et al., *supra.*, 1993), to act as an artificial transcription promoter (Mollegaard, *Proc. Natl. Acad. Sci. U.S.A.* 91:3892-3895, 1994) and as a pseudo restriction endonuclease (Demidov et al., *Nucl. Acids. Res.* 21:2103-2107, 1993). Recently, PNA has also been shown to have antiviral and antitumoral activity mediated through an antisense mechanism (Norton, *Nature Biotechnol.*, 14:615-619, 1996; Hirschman et al., *J. Investig. Med.* 44:347-351, 1996). PNAs have been linked to various peptides in order to promote PNA entry into cells (Basu et al., *Bioconj. Chem.* 8:481-488, 1997; Pardridge et al., *Proc. Natl. Acad. Sci. U.S.A.* 92:5592-5596, 1995).

The antisense oligonucleotides contemplated by the present invention can be administered by direct application of oligonucleotides to a target using standard techniques well known in the art. The antisense oligonucleotides can be generated within the target using a plasmid, or a phage. Alternatively, the antisense nucleic acid may be expressed from a sequence in the chromosome of the target cell. It is further contemplated that the antisense oligonucleotide contemplated are incorporated in a ribozyme sequence to enable the antisense to specifically bind and cleave its

target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., *Pharmacol. Ther.* 50(2):245-254, (1991), which is hereby incorporated by reference. The present invention also contemplates using a retran to introduce an antisense oligonucleotide to a cell. Retron technology is exemplified by U.S. Patent No. 5,405,775, which is hereby incorporated by reference. Antisense oligonucleotides can also be delivered using liposomes or by electroporation techniques which are well known in the art.

The antisense nucleic acids of the present invention can also be used to design antibiotic compounds comprising nucleic acids which function by intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. The sequences identified as required for proliferation in the present invention, or portions thereof, can be used as templates to inhibit microorganism gene expression in individuals infected with such organisms. Traditionally, homopurine sequences were considered the most useful for triple helix strategies. However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences based on the sequences of the present invention that are required for proliferation are contemplated for use as antibiotic compound templates.

The antisense oligonucleotides of this example employ the identified sequences of the present invention to induce bacterial cell death or at least bacterial stasis by inhibiting target gene translation. Antisense oligonucleotides containing from about 8 to 40 bases of the sequences of the present invention have sufficient complementary to form a duplex with the target sequence under physiological conditions.

To kill bacterial cells or inhibit their growth, the antisense oligonucleotides are applied to the bacteria or to the target cells under conditions that facilitate their uptake. These conditions include sufficient incubation times of cells and oligonucleotides so that the antisense oligonucleotides are taken up by the cells. In one embodiment, an incubation period of 7-10 days is sufficient to kill bacteria in a sample. An optimum concentration of antisense oligonucleotides is selected for use.

The concentration of antisense oligonucleotides to be used can vary depending on the type of bacteria sought to be controlled, the nature of the antisense oligonucleotide to be used, and the relative toxicity of the antisense oligonucleotide to the desired cells in the treated culture. Antisense oligonucleotides can be introduced to cell samples at a number of different concentrations preferably between 1×10^{-10} M to 1×10^{-4} M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use *in vivo*. For example, an inhibiting concentration in culture of 1×10^{-7} translates into a dose of approximately 0.6 mg/kg body weight. Levels of oligonucleotide approaching 100 mg/kg body weight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the subject are removed, treated with the antisense oligonucleotide, and reintroduced into the subject. This range is merely illustrative and one of skill in the art are able to determine the optimal concentration to be used in a given case.

After the bacterial cells have been killed or controlled in a desired culture, the desired cell population may be used for other purposes.

EXAMPLE 41

The following example demonstrates the ability of an *E. coli* antisense oligonucleotide to act as a bactericidal or bacteriostatic agent to treat a contaminated cell culture system. The application of the antisense oligonucleotides of the present invention are thought to inhibit the translation of bacterial gene products required for proliferation.

The antisense oligonucleotide of this example corresponds to a 30 base phosphorothioate modified oligodeoxynucleotide complementary to a nucleic acid involved in proliferation, such as Molecule Number EcXA001. A sense oligodeoxynucleotide complementary to the antisense sequence is synthesized and used as a control. The oligonucleotides are synthesized and purified according to the procedures of Matsukura, et al., Gene 72:343 (1988). The test oligonucleotides are dissolved in a small volume of autoclaved water and added to culture medium to make a 100 micromolar stock solution.

Human bone marrow cells are obtained from the peripheral blood of two patients and cultured according standard procedures well known in the art. The culture is contaminated with the K-12 strain of *E. coli* and incubated at 37°C overnight to establish bacterial infection.

The control and antisense oligonucleotide containing solutions are added to the contaminated cultures and monitored for bacterial growth. After a 10 hour incubation of culture and oligonucleotides, samples from the control and experimental cultures are drawn and analyzed for the translation of the target bacterial gene using standard microbiological techniques well known in the art. The target *E. coli* gene is found to be translated in the control culture treated with the control oligonucleotide, however, translation of the target gene in the experimental culture treated with the antisense oligonucleotide of the present invention is not detected or reduced.

EXAMPLE 42

A subject suffering from an *E. coli* infection is treated with the antisense oligonucleotide preparation of Example 39. The antisense oligonucleotide is provided in a pharmaceutically acceptable carrier at a concentration effective to inhibit the translation of the target gene. The present subject is treated with a concentration of antisense oligonucleotide sufficient to achieve a blood concentration of about 100 micromolar. The patient receives daily injections of antisense oligonucleotide to maintain this concentration for a period of 1 week. At the end of the week a blood sample is drawn and analyzed for the presence or absence using standard techniques well known in the art. There is no detectable evidence of *E. coli* and the treatment is terminated.

EXAMPLE 43

Preparation and use of Triple Helix Probes

The sequences of microorganism genes required for proliferation of the present invention are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches that could be used in triple-helix based strategies for inhibiting gene

expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into a population of bacterial cells that normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

The oligonucleotides can be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for a reduction in proliferation using techniques such as monitoring growth levels as compared to untreated cells using optical density measurements. The oligonucleotides that are effective in inhibiting gene expression in cultured cells can then be introduced *in vivo* using the techniques well known in that art at a dosage level shown to be effective.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (Science 245:967-971 (1989), which is hereby incorporated by this reference).

EXAMPLE 44

Identification of Bacterial Strains from Isolated Specimens by PCR

Classical bacteriological methods for the detection of various bacterial species are time consuming and costly. These methods include growing the bacteria isolated from a subject in specialized media, cultivation on selective agar media, followed by a set of confirmation assays that can take from 8 to 10 days or longer to complete. Use of the identified sequences of the present invention provides a method to dramatically reduce the time necessary to detect and identify specific bacterial species present in a sample.

In one exemplary method, bacteria are grown in enriched media and DNA samples are isolated from specimens of, for example, blood, urine, stool, saliva or central nervous system fluid by conventional methods. A panel of PCR primers based on identified sequences unique to various species of microorganisms are then utilized in accordance with Example 12 to amplify DNA of approximately 100-200 bases in length from the specimen. A separate PCR reaction is set up for each pair of PCR primers and after the PCR reaction is complete, the reaction mixtures are assayed for the presence of PCR product. The presence or absence of bacteria from the species to which the PCR primer pairs belong is determined by the presence or absence of a PCR product in the various test PCR reaction tubes.

Although the PCR reaction is used to assay the isolated sample for the presence of various bacterial species, other assays such as the Southern blot hybridization are also contemplated.

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 405-485, wherein said nucleic acid inhibits microorganism proliferation.

2. The nucleic acid sequence of Claim 1, wherein said nucleic acid sequence is complementary to at least a portion of a coding sequence of a gene whose expression is required for microorganism proliferation.

3. The nucleic acid sequence of Claims 1 or 2, wherein said nucleic acid comprises a fragment of one of SEQ ID NOs. 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

4. The nucleic acid sequence of Claim 3, wherein said nucleic acid sequence is complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

5. A vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 405-485.

6. The vector of Claim 5, wherein said promoter is active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

7. A host cell containing the vector of Claim 5 or Claim 6.

8. A purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242.

9. A fragment of the nucleic acid of Claim 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

10. A vector comprising a promoter operably linked to the nucleic acid of Claim 8 or Claim 9.

11. A purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

12. A purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters.

13. The nucleic acid of Claim 12, wherein said nucleic acid is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*,
5 *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

14. A purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having
10 a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

15. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

16. A host cell containing the vector of Claim 15.

17. A purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs.: 243-357, 359-398.

18. A purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs.
15 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

19. An antibody capable of specifically binding the polypeptide of Claim 17 or Claim 18.

20. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably
20 linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell.

21. The method of Claim 20, further comprising the step of isolating said protein.

22. A method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a
25 polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

23. A method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide having a sequence selected from the group consisting of 243-357, 359-398
30 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

24. The method of Claim 23, wherein said activity is an enzymatic activity.

25. The method of Claim 23, wherein said activity is a carbon compound catabolism activity.

26. The method of Claim 23, wherein said activity is a biosynthetic activity.

27. The method of Claim 23, wherein said activity is a transporter activity.

28. The method of Claim 23, wherein said activity is a transcriptional activity.

29. The method of Claim 23, wherein said activity is a DNA replication activity.

30. The method of Claim 23, wherein said activity is a cell division activity.

31. A method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

contacting said target with a candidate compound; and

measuring an activity of said target.

32. The method of Claim 31, wherein said target is a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA.

33. The method of Claim 32, wherein said target is a coding region of one of SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

34. A compound identified using the method of Claim 31.

35. A method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

36. The method of Claim 35, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

37. The method of Claim 36, wherein said cell is an *E. coli* cell.

38. The method of Claim 36, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

39. The method of Claim 35, wherein said antisense nucleic acid is transcribed from an inducible promoter.

40. The method of Claim 39, further comprising the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level.

41. The method of Claim 40, wherein said sub-lethal concentration of said inducer is such that growth inhibition is 8% or more.

42. The method of Claim 40, wherein said inducer is isopropyl-1-thio- β -D-galactoside.

43. The method of Claim 35, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.

44. The method of Claim 35, wherein said gene product is a polypeptide.

45. The method of Claim 35, wherein said gene product is an RNA.

46. The method of Claim 44, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

47. A compound identified using the method of Claim 35.

48. A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene.

49. The method of Claim 48, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof.

50. The method of Claim 49, wherein said proliferation inhibiting portion of one of SEQ ID NOs. 405-485 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

51. The method of Claim 48, wherein said compound is a triple helix oligonucleotide.

52. A preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

53. The preparation of Claim 52, wherein said proliferation-inhibiting portion of one of SEQ ID NOs. 405-485 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

54. A method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene.

55. The method of Claim 54, wherein said antisense nucleic acid is complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242.

56. The method of Claim 54, wherein said antisense nucleic acid is a sequence of one of SEQ ID NOs.: 405-485, or a portion thereof.

57. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.

58. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population.

59. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population.

60. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

61. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

62. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

63. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by electroporation.

64. The method of Claim 54, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

65. The method of Claim 54 wherein said antisense nucleic acid is an oligonucleotide.

66. A method for identifying bacterial strains comprising the steps of:

providing a sample containing a bacterial species; and

identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 405-485, 82-88, 90-242.

67. A method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

(c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and

(d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

68. A method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

- (a) identifying a gene or gene product required for proliferation in a first microorganism;
- (b) identifying a homolog of said gene or gene product in a second microorganism;
- (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;

(d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

(e) contacting the sensitized microorganism of step (d) with a compound; and

(f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

69. The method of Claim 68, wherein said step of identifying a gene involved in proliferation in a first microorganism comprises:

introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

70. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters.

71. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene.

72. The method of Claim 69, wherein the step of identifying a homolog of said gene in a second microorganism comprises expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism.

73. The method of Claim 69, wherein said inhibitory nucleic acid is an antisense nucleic acid.

74. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

75. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

76. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises directly contacting said second microorganism with said nucleic acid.

77. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises expressing an antisense nucleic acid to said homolog in said second microorganism.

78. A compound identified using the method of Claim 68.

79. A method of assaying a compound for the ability to inhibit proliferation comprising:

(a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

(c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and

(d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

80. The method of Claim 79, wherein said inhibitory nucleic acid is an antisense nucleic acid which inhibits the proliferation of said first microorganism.

81. The method of Claim 79, wherein said inhibitory nucleic acid comprises a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism.

82. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism.

83. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

84. A compound identified using the method of Claim 79.

85. A method for assaying compounds for activity against a biological pathway required for proliferation comprising:

sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

86. The method of Claim 85, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

87. The method of Claim 86, wherein said cell is an *E. coli* cell.

88. The method of Claim 85, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

89. The method of Claim 85, wherein said antisense nucleic acid is transcribed from an inducible promoter.

90. The method of Claim 89, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level.

91. The method of Claim 90, wherein said sublethal level of said antisense nucleic acid inhibits proliferation by 8% or more.

92. The method of Claim 90, wherein said agent is isopropyl-1-thio- β -D-galactoside (IPTG).

93. The method of Claim 91, wherein inhibition of proliferation is measured by monitoring the optical density of a liquid culture.

94. The method of Claim 85, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

95. A compound identified using the method of Claim 85.

96. A method for assaying a compound for the ability to inhibit cellular proliferation comprising:
contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and
determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

97. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

98. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antibiotic.

99. The method of Claim 96, wherein said cell contains a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell.

100. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid encoding the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed.

101. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

102. A compound identified using the method of Claim 96.

103. A method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

contacting said cell with an antibiotic, wherein the biological pathway on which said antibiotic acts is known; and

determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

104. A method for determining the pathway on which a test compound acts comprising:

(a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

(c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

105. The method of Claim 104, further comprising:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

106. A purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

107. A compound identified using the method of Claim 23.

108. A compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

109. A compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

110. A compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

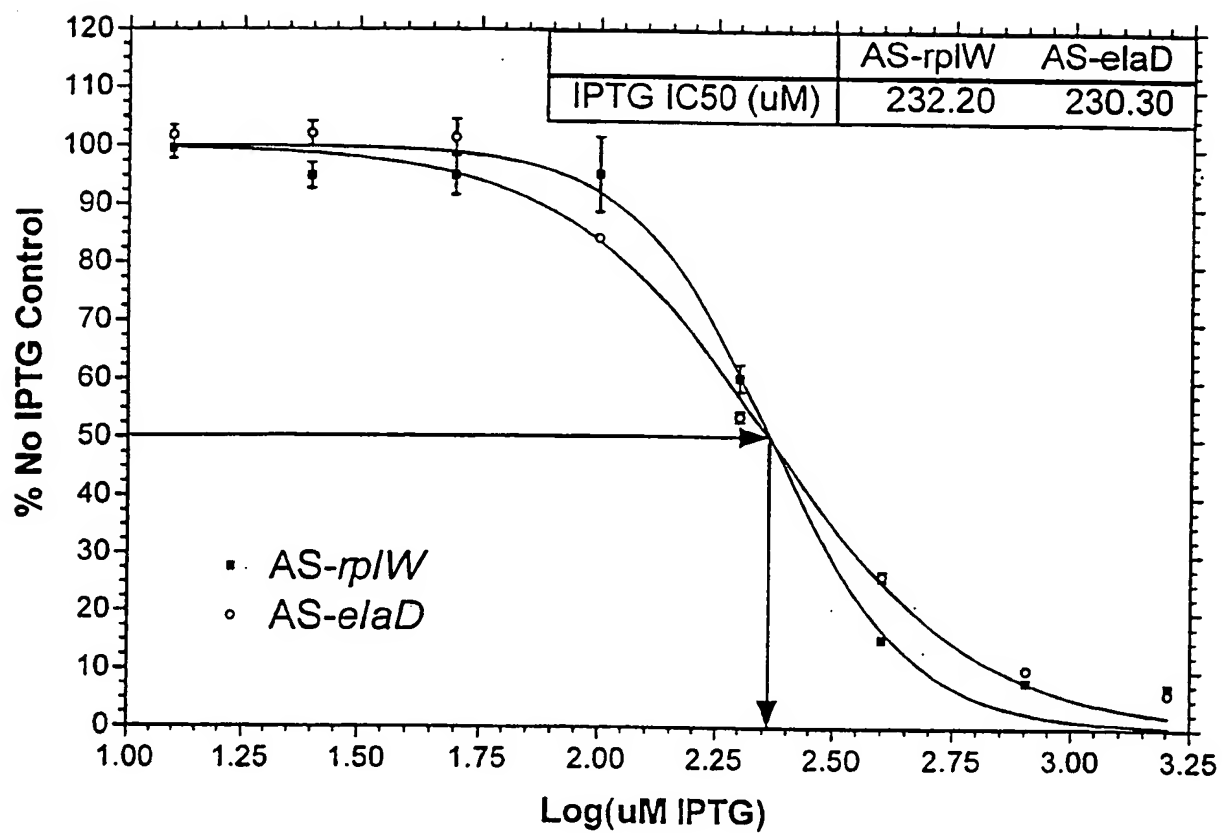
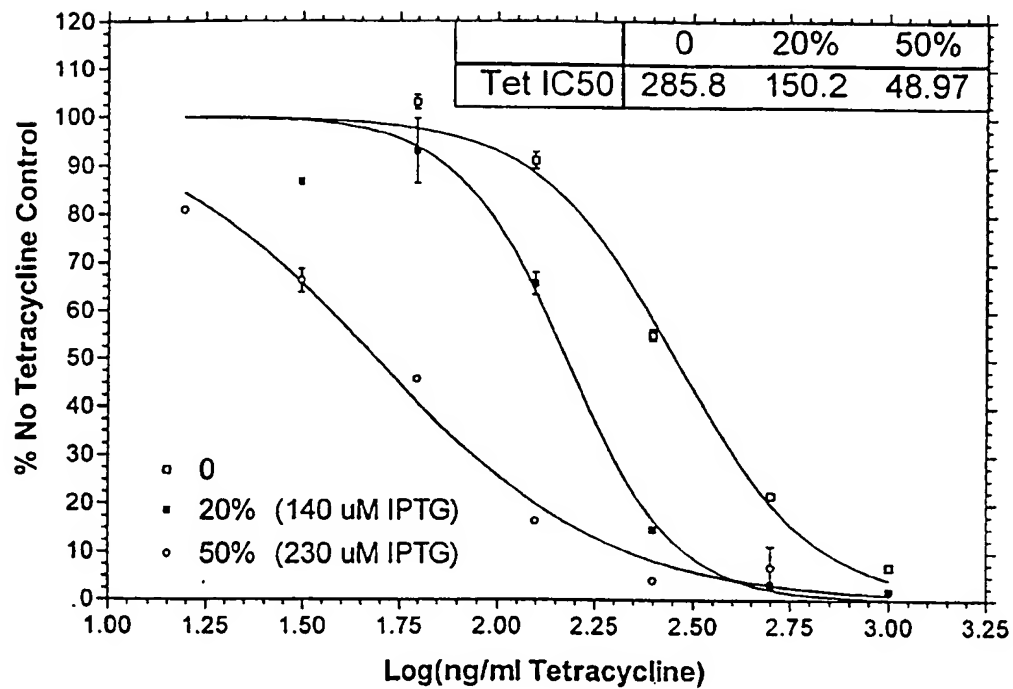
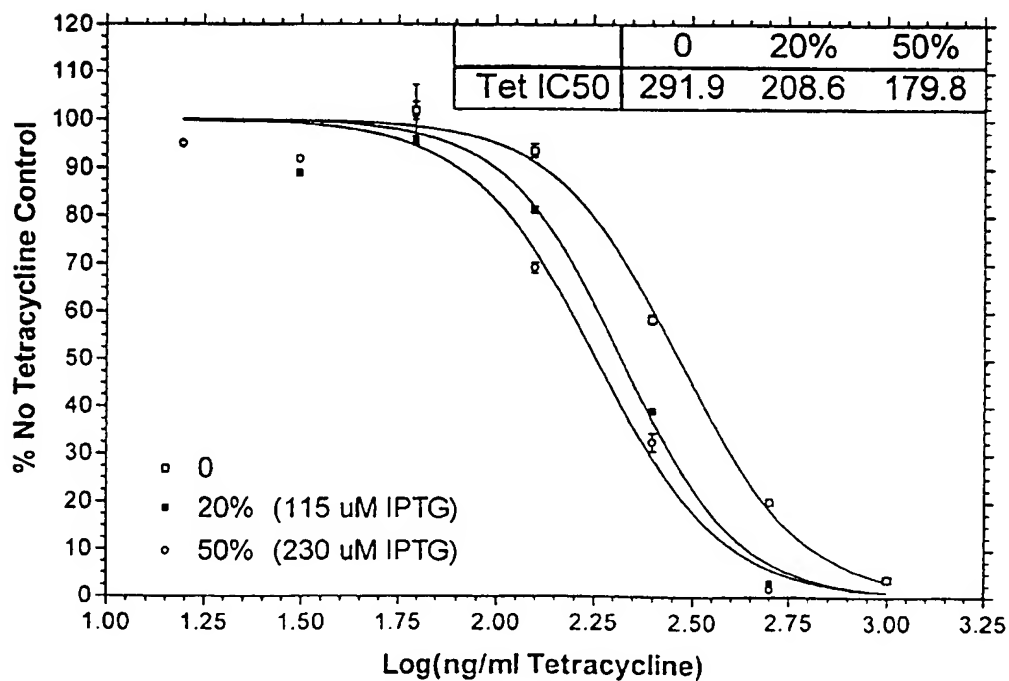


Fig. 1

AS-rplW**Fig. 2a****AS-elaD****Fig. 2b**

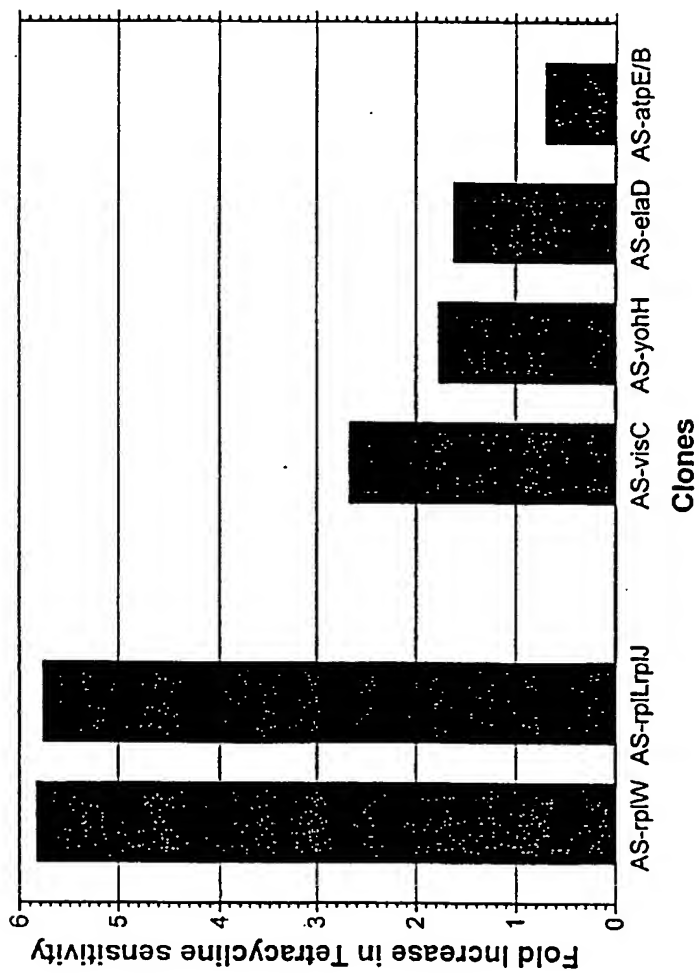


Fig. 3

SEQUENCE LISTING

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Zyskind, Judith
 Ohlsen, Kari L.
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gctgcaaccg	gaagggttgg	cttattttaac	ttcaacttca	gcgccagcct	cttccagagc	300
ttttttcagt	gcttctgcgt	cgtctttgct	cacgccttct	ttcagagcag	ccggtgcaga	360
ttctaccagc	tccttagctt	ctttcagacc	caggccagtt	gcg		403

<210> 7

<211> 149

<212> DNA

<213> E. Coli

<400> 7

gagctttttt	cagtgtctct	gcgtogtctt	tgctcacgcc	ttctttcaga	gcagccggtg	60
cagattctac	caggtcttta	gcttctttca	gacccaggcc	agttgcgcca	cgtactgctt	120
tgataacagc	aactttgtta	gcgccagca				149

<210> 8

<211> 742

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(742)

<223> n = A,T,C or G

<400> 8

ccatctgtcc	attgagcggg	cagtttgtgc	aacactatth	tggtgaccgg	aaaatggaac	60
actttccgca	atgcctgttg	ctatcacgct	ttaaccattt	cattgcat	tacacagaac	120
ggacgtcctg	tcgcagtata	ttaagtcgtc	gatagaaaca	agcattgaaa	ggcacagcag	180
tagtcaaaaca	gtgtgaaacg	ctactggcgc	cttacagcgc	aaaaaggctg	gtgactaaaa	240
agtcaccagc	catcagcctg	atthtctcagg	ctgcaaccgg	aagggttggc	ttatttaact	300
tcaacttcag	cgccagcttc	ttccagagct	tttttcagtg	cttctgcgtc	gtctttgtct	360
acgccttctt	tcagagcagc	cgggtgcagat	tctaccaggt	ctttagcttc	tttcagaccc	420
aggccagttg	cgccacgtac	tgctttgata	acagcaactt	tgtagcgcc	agcagctttc	480
agaattacgt	cgaattcagt	tnthtcttca	gcagcttcaa	ccgggccagc	agctacagct	540
acagcagcag	caagcggaaa	caccgaatth	ttcttccatt	gcagagatca	gttctacaac	600
cgtccattac	agacatagct	gcaactgctt	caatgattth	gatctttagt	ggatagacat	660
ttaaattgtt	cctgaattat	caagaaataa	gtnttatagc	taagccgaaa	tgcgtaaaaa	720
aagataactg	ngattaaagc	ag				742

<210> 9

<211> 421

<212> DNA

<213> E. Coli

<400> 9

agtagtcaaa	cagtgtgaaa	cgctactggc	gccttacagc	gcaaaaaggc	tggtgactaa	60
aaagtaccca	gccatcagcc	tgatttctca	ggctgcaacc	ggaagggttg	gcttatttaa	120
cttcaacttc	agcgccagct	tcttccagag	cttttttcag	tgcttctgcg	tcgtctttgc	180
tcacgccttc	tttcagagca	gccggtgcag	attctaccag	gtcttttagct	tctttcagac	240
ccaggccagt	tgccgccagt	actgctttga	taacagcaac	tttgtagcgc	ccagcagctt	300
tcagaattac	gtcgaattca	gttttttctt	cagcagcttc	aaccgggcca	gcagctacag	360
ctacagcagc	agcagcgga	acaccgaatt	tttcttccat	tgagagatc	agttctacaa	420
c						421

<210> 10
 <211> 126
 <212> DNA
 <213> E. Coli

<400> 10
 agagcctttt tcagtgttc tgcgtcgtct ttgtcacgc cttctttcag agcagccggt 60
 gcagattcta ccaggctctt agcttctttc agacccaggc cagttgcgcc acgtactgct 120
 ttgata 126

<210> 11
 <211> 262
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(262)
 <223> n = A,T,C or G

<400> 11
 ctgcaaccgg aagggttggc ttatttaact tcaacttcag cgccagcttc ttccagagct 60
 tttttcagtg cttctgcgtc gtctttgctc acgccttctt tcagagcagc cgntgcagat 120
 tctaccaggt ctttagcttc ttccagacc aggccagttg cgccacgtac tgctttgata 180
 acagcaactt tgttagcgcc agcagctttc agaattacgt cgaattcagt tttttcttca 240
 gcagcttcaa ccggggccagc ag 262

<210> 12
 <211> 202
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(202)
 <223> n = A,T,C or G

<400> 12
 gcgcataccc tgcagcatcg gcccgatgga gatcaggctg gcagaacgct gtaccgcttt 60
 gtaggtgggt ttaccgggtg tcagatccgg gaagatgaac acggtagcgc gacctgcaac 120
 cggagagttc ggcgctttgg attncgcaac gtcagccatt accgcagcgt cgtactgcag 180
 cggaccggcg atcatcaggt ca 202

<210> 13
 <211> 261
 <212> DNA
 <213> E. Coli

<400> 13
 tctaggagta agaatagctt caaattcagc agttgacagt ggcataaacg taactggtga 60
 cttttgcccg gcatgacgcc gggctttttt tattattccg tgacttccag cgtagtgaag 120
 gcaaaacttct cgccatcaaa tagccctga ctgggttagtt ttagcgcggt gatcactggc 180
 agagaaagaa acgcatctg aataaacggc tcatcggtga acggaccgca ttcacgggcg 240
 gcggccttca aggcgtcaat t 261

<210> 14
 <211> 224
 <212> DNA
 <213> E. Coli

<400> 14

ttcttttttt	cgtaacggt	gtccagaatc	atctttat	cttcggggt	cttatgctga	60
tttttattat	tatggggaag	gtgttattta	tgagtttcat	ttatgccgta	acgacaatga	120
actcggaat	tagtataagc	agcgcgagaa	taataatcat	tgtgcaaag	ctaattta	180
taatactatt	taaatattat	tttgagcata	tgacataag	gttg		224

<210> 15
 <211> 232
 <212> DNA
 <213> E. Coli

<400> 15						
aattcccttc	tttttttcgt	caacggtgtc	cagaatcatt	ttatttacct	cggtactta	60
tgctgatttt	tattattatg	gggaagggtg	tatttatgag	tttcatttat	gccgtaacga	120
caatgaactc	gggaattagt	ataagcagcg	cgagaataat	aatcattgtg	caaagtctaa	180
tttaattaat	actattttaa	tattattttg	agcatatgca	cataagggtg	gg	232

<210> 16
 <211> 212
 <212> DNA
 <213> E. Coli

<400> 16						
aatagcgggt	atgcacgcct	ttcttttttt	cgtaacggt	gtccagaatc	atctttat	60
cttcgggtac	ttatgctgat	ttttattatt	atggggaagg	tgttatttat	gagtttcatt	120
tatgccgtaa	cgacaatgaa	ctcggaatt	agtataagca	gcgcgagaat	aataatcatt	180
gtgcaaagtc	taatttaatt	aatactattt	aa			212

<210> 17
 <211> 433
 <212> DNA
 <213> E. Coli

<400> 17						
ccttgtaaat	tatcgcccg	ggcataaaaa	ctgcgtccaa	acgcggtctt	tgccagcagc	60
caggccataa	atgccaccag	aattatcgct	aaccaacca	ttgctgaaac	gccagcagc	120
agcggggcgg	agagctgttt	cagttcggcg	ggtaaccctt	caatccattt	gccgccagtc	180
cacagcaaca	tgatgcctct	gtacaaccct	aacgtgccaa	gggtggcaac	aatggcaggg	240
atcttttagc	acgcgaccag	gacaccgttg	aaaaatccc	cgagcaaac	aagcagtaaa	300
gtcgcgacac	aagcaacagg	tagtgaatat	cctgcgttca	gtaacatccc	caacagcacc	360
gcgcacattc	cggtaatcga	acccactgaa	acatcaatat	tgccgcgtaag	cattaccagc	420
gtcgcgcccc	ttg					433

<210> 18
 <211> 658
 <212> DNA
 <213> E. Coli

<400> 18						
cgtgcgcttc	cggttggtgc	aaccgcgcaa	atggcgcggc	ggtaagtatg	gcgggggttat	60
tccttccccg	ttgaggacac	cggttggtca	ggttgaccat	acgcttaagt	gacaaccccc	120
ctgcaacgcc	ctctgttatc	aattttctgg	tgacgttttg	cggtatcagt	tttactccgt	180
gactgctctg	ccgccctttt	taaagtgaat	tttgatgatg	ggatgaatgcg	gctgagcgca	240
cgcggaacag	ttaaaaccaa	aaacagtgtt	atgggtggat	tctctgtatc	cggcgttaat	300
tgtaactg	ttaacgtcac	ctggaggcac	caggcactgc	atcacaaaat	tcattgttga	360
ggacgcgata	atgaaaacgt	tattaccaaa	cgtaataacg	tctgaagggt	gttttgaaat	420
tggtgtcact	atcagtaacc	cagtatttac	tgaagatgcc	attaacaaga	gaaaacaaga	480
acgggagcta	ttaaataaaa	tatgcattgt	ttcaatgctg	gctcgtttac	gtctgatgcc	540
aaaaggatgt	gcacaatgaa	ttcagcattt	gtgcttggtc	tgacagtttt	tcttgtttcc	600
ggagagccag	ttgatattgc	agtcaagtgg	tcacaggaca	atgcaggagt	gtatgact	658

<210> 19

<211> 588
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(588)
 <223> n = A,T,C or G

<400> 19
 gtgactgctc tgccgccctt tttaaagtga attttgtgat gtggtgaatg cggctgagcg 60
 cacgcggaac agttaaaacc aaaaacagtg ttatgggtgg attctctgta tccggcggtta 120
 attgttaact ggtaacgctc acctggaggc accaggcact gcatacaaaa attcattggt 180
 gaggacgcga taatgaaaac gttattacca aacgttaata cgtctgaagg ttgttttgaa 240
 attggtgtca ctatcagtaa ccagtatatt actgaagatg ccattaacaa gagaaaacaa 300
 gaacgggagc tattaataaa aatatgcatt gtttcaatgc tggctcgttt acgtctgatg 360
 ccaaaaggat gtgcacaatg aattcagcat ttgtgcttgt tctgacagtt tttcttggtt 420
 ccggagagcc agttgatatt gcagtcagtg ttcacaggac aatgcangag tgtatgactg 480
 cagcaacccg aacagaaaat tcccggtaac tgttaccggc tcgataaagt tattcaccag 540
 gataatatcg aaatcccggc aggtctttaa aacagttccg taataaat 588

<210> 20
 <211> 101
 <212> DNA
 <213> E. Coli

<400> 20
 gatccagcaa gaagatgcgg ttgtaccgtc atcacgcaga tgcgcaaagc tactcagcaa 60
 ctgacctttc ttcgcaataa gcacgccatt agcgtcatag a 101

<210> 21
 <211> 465
 <212> DNA
 <213> E. Coli

<400> 21
 tcgcgtgttt accttcaaca tcggtaactt tctggcggat agtttcacgg taagcaacct 60
 gcgggtttacc tacgttcgct tcaacgttga attcacgctt catacgggtca acgatgatgt 120
 cgagggtgcaag ttgcgccata ccgcgcatga tggctctggt agattcttcg tcagtcata 180
 cacggaaaaga cgggtcttct ttagccagac ggcccagagc cagaccatt ttttcctggt 240
 cagctttggt tttcggttca actgcgatgg agattaccgg ctcagggaat tccatacgtt 300
 ccagaatgat cggcgcaccc gggtcacaca ggggtgtcacc agtgggttacg tctttcagac 360
 cgatagcagc agcgtatgtc cccgcgcgaa cttctttgat ctcttcacgt ttgttagcgt 420
 gcacttgaac gatacgaccg aaacgctcac gtgcagcttt cacgg 465

<210> 22
 <211> 859
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(859)
 <223> n = A,T,C or G

<400> 22
 tgatcggtc aagcagaact ggtttcgctt tcttaaagcc ttctttaag gcgatagaag 60
 cagccagttt aaacgccagt tcagaggagt caacgtcatg gtaagaaccg aagtgcagac 120
 gaatacccat gtctactacc ggtagcctg ccagcggacc tgctttcagc tgttcctgga 180
 tacctttatc aacggccggg atgtattcgc cagggattac accaccttta atgtcgttga 240
 tgaactcgta gcctttcggg tttgaacccg gctccagcgg gtacatgtcg ataacaacat 300

gaccatactg	accacgacca	ccagactggt	tcgctgtgtt	accttcaaca	tcggtaactt	360
tctggcggat	agtttcacgg	taagcaacct	gcggtttacc	tacgttcgct	tcaacgttga	420
attcacgctt	catacgggtca	acgatgatgt	cgaggtgcag	ttcgcccata	ccgcgatga	480
tggctctggt	agattcttcg	tcagtccata	cacggaaaga	cgggtcttct	ttagccagac	540
gggcanagc	cagaccatt	tttctctggt	cagctttggt	tttcggtcaa	ctgcgatgga	600
gattaccggc	tcanggaatt	tccatacctt	ccaggaatga	tcggcgcat	ccggtcaaac	660
angngtacc	aggggggtac	ntntttttaa	nancgattgc	cagcancgga	tntnnccgn	720
gccnaacttc	tttgaacnn	tttaccggtt	ggtaaccngc	cttttnaacn	atccaaccga	780
aaaagngtta	anngccantt	ttccngnggt	tnanntncgg	nttccngaa	ntaaccncc	840
cggggtnaac	ccngnaaaa					859

<210> 23

<211> 269

<212> DNA

<213> E. Coli

<400> 23

ctttcttaaa	gccttcttta	aaggcgatag	aagcagccag	tttaaaccgc	agttcagagg	60
agtcaacgtc	atggtaagaa	ccgaagtgc	gacgaatacc	catgtctact	accgggtagc	120
ctgccagcgg	acctgctttc	agctgttcct	ggataccttt	atcaacggcc	gggatgtatt	180
cgccagggat	tacaccacct	ttaatgtcgt	tgatgaactc	gtagcctttc	gggtttgaac	240
ccggtccag	cgggtacatg	tcgataaca				269

<210> 24

<211> 330

<212> DNA

<213> E. Coli

<400> 24

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgacccctc	tgttcttata	acacaaggaa	acgtacttaa	ggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggcgtaag	gcttcccagt	300
aatataatta	atactctact	tccagagtag				330

<210> 25

<211> 471

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(471)

<223> n = A,T,C or G

<400> 25

gttttgggga	gatgtaagg	ctaactctgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgacccctc	tgttcttata	acacaaggaa	acgtacttaa	ggtgccgtcc	ggtgaaccag	180
tcggacgcac	ctttaataac	tataaataag	tgctctgggc	gatactatat	aaattaactt	240
agtgaatgat	tatgctaattg	tcattcaatta	aataaatata	atggcgtaaa	ggcttcccag	300
taatataatt	aatactctac	ttccagagta	gaatattaaa	ttttatccgc	gtggtgcac	360
agcacaaatt	tatcccacaa	ctgttcttct	gtctcgacat	gccccccgat	cttnacaaa	420
tantattggg	ggattnggcc	cncctttttg	ncagggttgg	gtcntctnat	g	471

<210> 26

<211> 379

<212> DNA

<213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(379)
 <223> n = A,T,C or G

<400> 26
 natctgantg gctgcattcc ttgtttaagg aaacccgaat gactgattgc cgatacctga 60
 ttaaacgggt catcaaaatc atcattgctg ttttacagct gatccttctg ttcttataac 120
 acaaggaaac gtacttaagg tgcgtccggt gaaccagtcg gacgcacctt taataactat 180
 aaataagtgt ctgggcagat actatataaa ttaacttagt gaatgattat gctaagtgtca 240
 tcaattaaat aaatataatg gcgttaaggc ttcccagtaa tataattaat actctacttc 300
 cagagtagaa tattaaattt tatccgcgtg gtgcatacgc acaaatattat cccacaactg 360
 ttcttctgtc tcgacatgc 379

<210> 27
 <211> 799
 <212> DNA
 <213> E. Coli

<400> 27
 aaagatgatg tgatgagaaa gtcaatttga ataagacaat attaagagct aaaaaaatgt 60
 caaaaaacac taaatcaaaa aataatggca tttagaaaata taatgcgaaa acggagggtga 120
 aattagttaa tttcaaatga ggaaaatctc ccggcgaaaa aaccgggaga tgaaaagtgtg 180
 atgggtrata aataaacaac agaggagaaa tttttaacgc agccattcag gcaaatcgtt 240
 taatcccatg gcctggcgga taagttagcg cttaacgcca ggaagcgtgt cggccagtgt 300
 caaaccaata tcacgcagca gttttttcgc cggatttggt cgggaaaaca gatcgcgga 360
 tccttgcata ccagccagca tcaacgcgc actgtgctt cggctacgt catagcgacg 420
 cagataaatg tactgcccga tgtctgggat ccgtcgacct gcagccaagc ttgggctttt 480
 cagcctgata cagattaaat cagaacgcag aagcgggtct ataaaaacaga atttgcctgg 540
 cggcagtagc gcgggtggtcc cacctgaccc catgccgaac tcagaagtga aacgcccgt 600
 gcgcccagtg gtagtgtggg gtctcccat gcgagagtag ggaactgcca ggcatacaat 660
 aaaacgaaag gctcagtcga aagactgggc ctttcggtt atctgggtgg tgtcggtgaa 720
 cgctctctga gtaggacaaa tccgccggga gcggattttg aacgttgcca aacaaccggc 780
 ccggaaaggg gtggggggt 799

<210> 28
 <211> 636
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(636)
 <223> n = A,T,C or G

<400> 28
 aggggggttt ttgtgggcaa tgatgcattt aagttatcgt ctgcagatag aggagatatt 60
 acaataaaca acgaatcagg gcatttgata gtcaataccg caattctatc aggagatata 120
 gtcactctaa gaggaggaga aattagggtt gtattatagc ttgtgcgcgc catgattggc 180
 gcgcaattta aacttagtgc tttacatcgc tattgtcttg atttctttga attattttat 240
 aaattaaaaa aacgactgtt atgtataagc aaaggctcga cgaaaaatc attccaaata 300
 aatgcttgct taaatctcta tatccttccc cgaaaaatga cacataaaat tgagatattc 360
 caaaaagaga tactacaaat aaagatgcct ttattttatt atttctaata aaaatagaag 420
 caataaaaaa taataacaat gatataaatc taatgttttt aaatatattg tcttttatgt 480
 tagtaatagt cgttagtatg tttgattctc catatattac gtgtagtttt ttatatacat 540
 ggaaataatt ntctttatc tgagacatca caccatcacc aaatggaagt ttgaagatgg 600
 tgcttggttt gctaaccaat aaaaagagtg cattcg 636

<210> 29
 <211> 757
 <212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(757)

<223> n = A,T,C or G

<400> 29

cagcggtcgt	attttttagca	tggtttttta	ttggcggcta	tgctgccccg	ggagcataaa	60
gatgaaaaaa	acaacgatta	ttatgatggg	tgtggcgatt	attgtcgtac	tcggcactga	120
gctgggatgg	tggtaacgtc	acctctaaaa	aatagcaaag	gctgcctgtg	tgcagccttt	180
gtgcaattta	agcgttaact	tttaatcttc	ctgtagataa	atagcacgac	aatcgcacca	240
ataacggcaa	ccacgaagct	gccaaaattg	aagccatcga	ctttaccaaa	gccaaaacagc	300
gtgctgatcc	atccgcccgc	tacggcacccg	actatcccca	gcaggatagt	cataaagaat	360
ccacctccat	ctttacctgg	catgatccac	ttcgccagaa	taccggcaat	aagcccaaaa	420
ataatccatg	acagaatgcc	cattgtttcc	tcacttatot	gttttgcat	agcgggttag	480
tcgctgataa	aaagcatagc	acaacatcgg	gagggcaaga	tttgtgacga	gcatacacgga	540
ggtttttttt	gcgatggcgc	agaaattgcg	ccatcaacga	tcagtgataa	ttaccaacca	600
caaacatcat	gttcgttttc	cgtgtcataa	gaaccgtacg	ggattcacca	gatcttttat	660
cacttcaagc	cggcactttc	ggcaccagca	aagtcacggg	cgtctctggt	tcataatcga	720
ccggaaacgc	cattgctggt	attggtgaen	gtcacgg			757

<210> 30

<211> 392

<212> DNA

<213> E. Coli

<400> 30

aattacagaa	aaaggaggca	atatcgggta	aaggcattag	cccgcgaat	acgtcgggct	60
acaaatatta	ttgtgctgca	ggtgttttag	cgggttggtg	atccacaggt	tctaactgga	120
agaccacatc	gacctgatca	tcaaactgaa	tagcggcctg	ctcgtaagtt	tcctgggcgg	180
acaccggcgc	ggcatcggct	ttcatcatcc	gcaccattgg	gctgggctga	tagttggaaa	240
catggtagcg	cacgctatat	accggcccca	gtttacgatg	aaagccgttc	gccagttcct	300
gcgcctgatg	aatcgcggtt	tcaatcgctg	ccttacgcgc	tttgtcttta	taggcatccg	360
gctgcgccac	gccagcgac	acagaacgaa	tt			392

<210> 31

<211> 351

<212> DNA

<213> E. Coli

<400> 31

ctatccttga	tgaaacgcgc	agcaaagata	ggtgattacg	tcattggtttt	acagaaaatt	60
acagaaaaag	gaggcaatat	cgggtaaaag	catttagccc	acgaatacgt	cgggctacaa	120
atattattgt	gctgcagggt	ttttagcggg	ttgttgatcc	acaggttcta	actggaagac	180
cacatcgacc	tgatcatcaa	actgaatagc	ggcctgctcg	taagtttcct	ggcggaacac	240
cggcgcgcca	tcggctttca	tcatccgcac	cattgggctg	ggctgatagt	tggaaacatg	300
gtagcgcacg	ctatataccg	gccccagttt	acgatgaaa	ccgttcgcca	g	351

<210> 32

<211> 762

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(762)

<223> n = A,T,C or G

<400> 32

aattatgaaa	cactgtctgg	aatcgtctga	atgacgggca	catttgcgag	cacgcatcca	60
------------	------------	------------	------------	------------	------------	----

gtaataaacac	aggaaactat	tttatctacg	cgttagcgat	agactgcttg	catggcgaaa	120
ggaggttaagc	cgacgatttc	agcgggacgc	tgaacggga	aagcccctcc	cgaggaaggg	180
gccataaata	aggaaaggg	catgatgaag	ctactcatca	tcgtggtgct	cttagtcata	240
agcttccccg	cttactaaga	ctaccagggc	gggggaaacc	ccgctctacc	ctcactcctg	300
aaagtatgcc	ttcacgataa	gattgtcaat	ccgcaggctt	tgtagtctgc	gatcctgcc	360
gcaaatattc	tttgcgagtc	gttacgcaat	aatcacagag	gaaactat	tattcacgcg	420
ttagcgatag	actgcattca	gggcgaaagg	aggtaagccg	atgatttcag	cgggacgctg	480
aaacgggaaa	gcctctcccg	gagaagaggg	cttttaataa	ggaaaggggt	atgatgaagc	540
acgtcatcat	actggtgata	ctcttagtga	ttagcttcca	ggcttactaa	gaacaccagg	600
gggaggggga	aacctcttcc	taaccctcac	ttctgaaatt	gggtgctatg	acgctggcgt	660
tactgcttan	cgctaccagt	ttgtctgccc	tggcggttgt	aacgccagat	cggtaccctg	720
ttggatattt	taatgaaagc	cgacaaatca	atcancgtga	cg		762

<210> 33
 <211> 293
 <212> DNA
 <213> E. Coli

<400> 33						
gcacatttgc	gagcacgcat	ccagtaataa	cacaggaac	tattttatct	acgcgttagc	60
gatagactgc	ttgcatggcg	aaaggaggt	agccgacgat	ttcagcggga	cgctgaaacg	120
ggaaagcccc	tcccaggagaa	ggggccataa	ataaggaaag	ggatcatgat	aagctactca	180
tcatcggtgt	gctcttagtc	ataagcttcc	ccgcttacta	agactaccag	ggcgggggaa	240
accccgctct	accctcactc	ctgaaagtat	gccttcacga	taagattgtc	aat	293

<210> 34
 <211> 633
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(633)
 <223> n = A,T,C or G

<400> 34						
atttacactt	tttacgaaat	catgggatca	ctaacaaaat	atcgcttgct	agttatatgt	60
tatggcagga	aagatatgct	actgatatta	cagatcccca	aagtggagag	tttatgacca	120
ttaaaaataa	gatgttgctg	ggtgcgcttt	tgctggttac	cagtgcgcgc	tgggccgcac	180
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	240
ttgctgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	300
agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	360
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	420
cctacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	480
tcagacacac	ttgntatttt	ttattattag	ccacttgctc	gtcttgcttg	gtattaagtc	540
gtatttccag	ttgattaatg	cnggtggctc	cagtgcgcga	gattaacttt	gtttggatcg	600
aagacgtagt	aactggctgg	ttatcggaat	tgg			633

<210> 35
 <211> 569
 <212> DNA
 <213> E. Coli

<400> 35						
tatggcagga	aagatatgct	actgatatta	cagatcccca	aagtggagag	tttatgacca	60
ttaaaaataa	gatgttgctg	ggtgcgcttt	tgctggttac	cagtgcgcgc	tgggccgcac	120
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	180
ttgctgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	240
agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	300
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	360
cctacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	420

tgcagacacc	ttgttatttt	ttattattag	ccacttgctc	gttttgcttg	ttattagtcg	480
tatttcacgt	tgattaatgc	ggttgcctcc	agtgcgccag	atttaacttt	gtttgtatcg	540
tagacgtagt	aactggctgg	tatcggaaat				569

<210> 36
 <211> 338
 <212> DNA
 <213> E. Coli

<400> 36						
cgtattcaca	tccttttgat	tggtgataac	atgcgaatcg	gtattatttt	tccggttgta	60
atcttcatta	cagcggtcgt	attttttagca	tggtttttta	ttggcggcta	tgctgccccg	120
ggagcataaa	gatgaaaaaa	acaacgatta	ttatgatggg	tgtagcgatt	attgtcgtac	180
tcggcactgc	ctgggatggg	ggtaacgtca	cctctaaaaa	atagcaaagg	ctgcctgtgt	240
gcagcctttg	tgcaatttaa	gcgttaactt	ttaatcttcc	tgtagataaa	tagcacgaca	300
atcgaccaa	taacggcaac	cacgaagctg	ccaaaatt			338

<210> 37
 <211> 375
 <212> DNA
 <213> E. Coli

<400> 37						
ctgaatat	aaaaaggaaa	acgacatgaa	accgaagcac	agaatcaaca	ttctccaatc	60
ataaaatatt	tccgtggagc	attttattat	tgaatataga	ggtttaactc	cggtaaaaaa	120
caaagaagca	ttgaatgcag	ggaaaaataa	tatggccata	aaaaacatcg	aaagaaactc	180
ttttaattta	acatgtaaac	gcatggttaa	tcctcatatc	acgggtggag	tgtaagaac	240
atacataaat	ggagtcattg	tttccctttt	ccatttatca	agttcctgtt	gccgttttag	300
tccatctcta	attgcatatt	ttaatttttc	tgataaatgg	cattgagcat	cgatttcatt	360
taaaacaact	gtaca					375

<210> 38
 <211> 446
 <212> DNA
 <213> E. Coli

<400> 38						
ttacgatagc	tattagtaaa	aataaagag	ttagctgtat	tgttatgtct	gtggcgaaat	60
tgactacatt	cgtttttttg	attaagaatg	attttattat	cgtaagttaa	attacatgaa	120
tatttaaaaa	ggaaaacgac	atgaaaccga	agcacagaat	caacattctc	caatcataaa	180
atatttccgt	ggagcatttt	attattgaat	atagaggttt	aactccggta	aaaaacaaag	240
aagcattgaa	tgcagggaaa	aataaatatg	ccataaaaaa	catcgaaaga	aactctttta	300
atttaacatg	taaacgcatg	gttaatcctc	atatcacggg	tgagtggtta	agaacataca	360
taaatggagt	catgttttcc	cttttccatt	tatcaagttc	ctgttgccgt	tttagtccat	420
ctctaattgc	atattttaat	ttttct				446

<210> 39
 <211> 392
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(392)
 <223> n = A,T,C or G

<400> 39						
tcaccccggt	gccgattttc	aggcatcctg	atttaactta	gcacccgcaa	cttaactaca	60
ggaaaaacaaa	gagataaatg	tctaactcctg	atgcaaatcg	agccgatttt	ttaatcttta	120
cggacttttta	ccgcctgggt	ttattaattg	cactgtnatc	cggcggttcg	cccgttttaa	180
tcacaatagg	ctgtgtagcc	tgggcctggt	tctctttcac	ccgcgccaga	gcggcagcaa	240

tcgcaccttt atctttggct gcaggttgaa cggctgcgt cttatgtcgt tcaaggcgag	300
ccgcttttc gcgctccaga cgagcctggc gcgcttcgaa acgcgcttg gcttctgcgg	360
cncgcttttc ttcctgacga atagccgcaa tt	392

<210> 40
 <211> 208
 <212> DNA
 <213> E. Coli

<400> 40	
taataacgct atctgcggat aaagcagaat aggtgggttaa cccagacat aaaccgagga	60
aaataatggt attgtatttc ataacttatt gttccttagc gacagattgc tgtctgctgg	120
ttcagtaagg taccagaga aacttcagga agcttgtagt cgacaatata gtttgagttt	180
ttatctttgc cccatgaaac ctgtaatt	208

<210> 41
 <211> 342
 <212> DNA
 <213> E. Coli

<400> 41	
catectcaat accgttaaata gcaacccgaa ccccggtgt ccctttgctg cattcactta	60
acgtaatctg aaaagggacg gctggacttg tgctaccggt cggtggaaat tgtctggcac	120
tggttttttg gagatctacg gtaaaattaa gcgaatccga tgagactgtg cagccataat	180
cgaggacgcg cccgctaatt ttaataacgc tatctgcgga taaagcagaa taggtgggta	240
accccagaca taaaccgagg aaaataatgt tattgtattt cataatctat tggtccttag	300
cgacagattg ctgtctgctg gttcagtaag gtaccaggag aa	342

<210> 42
 <211> 841
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(841)
 <223> n = A,T,C or G

<400> 42	
agatttactg ccaatttccg gcagatcgga aagggttaaa ccatattgat ccataagggg	60
acgaatcacg gctataccgc caggcatggc ttgagccatg gcattaaatt ccgcaaattc	120
gggcgctgat tcttcccacg cgggtatttt ggcacacacc agatccagca aggggttntc	180
aggatcggtg agcagcagat gatctaccag ttncagcgcc tgggtgtatt gntccttggt	240
ctgaataccc gnnagaaaag gtgccacagc anttagcttn tctcctgctt gcaagatgtc	300
tggcaatngc aatcattttt tgcacttant acgatgnaca ncngtaaaga aatcgnattt	360
ttntatgccg tcataacttt acgtatgtan cactttttgc nattcnaaaa aagaccattn	420
gctncaacac gtaaatattna ttgncccccna catttanaac ataaatgntt aaaattttcc	480
ccccnccnnan ttttaagntn ttnanagaat ngggaattac ctgctttttna atgnactcan	540
anttttttng naataattcc tntatcnaa ctnntttttn cccaanagnc nnccaaattn	600
cggtttnttn nttnnccnng cnttttttta cccnanaann tttattcaan nccttttttg	660
tagnctatatt naagnggnet ttnttnnatt aactttccnn ttggncaaat tttggcnnat	720
ttttatatan aattntctta tntcntaatt tnggnanccc cngatgnaan tttatggngg	780
gantcccnnt cctnttttaa ttnatgntct gggntatttt taaancctnn attaanannan	840
c	841

<210> 43
 <211> 215
 <212> DNA
 <213> E. Coli

<400> 43

aataactttt	cgtaggcag	tttgggtgt	gagttgcaag	aggggagact	actgaataac	60
tcaagtttta	taatcgagg	gaaaatggtg	atggcgttca	tagcaaaacg	ccctcaacca	120
taaaggctga	gggcgcttaa	gatgttaaaa	acccgctatc	cgtaaaaaaa	caatgttcaa	180
ctaaggctcag	tgacattgcg	ctaaaaaagc	gaatt			215

<210> 44
 <211> 395
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(395)
 <223> n = A,T,C or G

<400> 44						
gcattattca	tgagaaatgt	gtatcgtaaa	tcaactgaaa	ttaacgcaac	catttgttat	60
ttaaggttta	attatctgtg	tgtgataattt	tattgaatgt	tttaaattatt	gtttttattg	120
gcattgctat	aattattggtt	atcatttgct	gaatggattc	agtcttaattg	agtgggtttt	180
taagggacag	gcatagagta	atgatacgta	tgcataacca	acatctttac	tcattatgtc	240
attgaatgtt	gaccctatgt	gtttatgaag	gagaggtatt	ttcagttgat	ctggattgnt	300
aaattcatat	aatgcgcctt	tgctcatgaa	tggtatgccag	tatgtagtgg	gaaattataa	360
atattgaaat	agtccaacta	cttctttatt	accaa			395

<210> 45
 <211> 883
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(883)
 <223> n = A,T,C or G

<400> 45						
ataatcaggt	aagaaaaggt	gcgcggagat	taccgtgtgt	tgcgatatat	tttttagttt	60
cgcgtygcaa	tacatcagtg	gcaataaaaac	gacatatcca	gaaaaatata	cactaagtga	120
atgatatctt	ccgatttatc	ttaatcgttt	atggataacg	gcaaagggtc	tcgttttttc	180
ctatacttat	tcagcactca	caaataaagg	aacgccaatg	aaaattatac	tctgggctgt	240
attgattatt	ttcctgattg	ggctactggg	ggtgactggc	gtatttaaga	tgatatttta	300
aaattaatta	atgtcatcag	gtccgaaaat	aacgagaata	tttcagtctc	tcatcctggt	360
gcgctcctgt	catgtgcatt	gcttcatata	atcactggcg	caaggagcgc	cgcaggcgna	420
gnntgcncgn	cgneccacct	naccccatgc	cgaacttcag	aantgaaaac	nccntaacnc	480
cgatngtcgg	cggnggcctc	cccatgcnan	agtangggaa	ntgccangcg	ncnnattaaa	540
cgaaaggctn	attncaaaga	ctgggccttn	cntttatctg	atgtttgtcg	gagaacgctc	600
tcctgagnan	gacaaatncc	gccgggagcg	gatttgaacn	ttgcgaagca	accgnccna	660
aggngnngt	cntgacnccc	nnctctant	nnngccttc	ttttgcttna	angncctcct	720
ancngatggc	ctttttngcc	ntctacaaa	cnntttggtt	aatgcttnta	aaancctttc	780
cannntncaa	tcngtnntn	cccatccnnn	tnntgaaagn	ntnccntccn	tgtncantnt	840
anntnngggg	gnngngngcc	ggcggncccc	ccccccccc	ccc		883

<210> 46
 <211> 1024
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(1024)
 <223> n = A,T,C or G

<400> 46

gtttatggat	aacggcaaaag	ggcttcggtt	tttcctatac	ttattcagca	ctcacaata	60
aaggaacgcc	aatgaaaatt	atactctggg	ctgtattgat	tattttcctg	attgggctac	120
tggtggtgac	tggcgtattt	aagatgatat	tttaaaatta	attaatgtca	tcagggtccga	180
aaataacgag	aatatttcag	tctctcatcc	tgttgcgctc	ctgtcatgtg	cattgcttca	240
tataatcact	ggcgcaagga	gcgcgcagag	tctccnant	nnnnntnntt	ntntnnctnn	300
nccttcacna	tncnccnncn	nantnnatag	nncaccnntn	tnntcnnnnn	gncncctcc	360
nnncnnnnnn	ncatnnnatc	ccactnnntt	tctccannn	nnncnnnntn	cancnacaa	420
antncnaccn	anntnacctt	atacnannnc	nancnnnnnn	nnccactctn	nctcgnnctc	480
cccnttcnac	nnccannnnn	cancnntcnn	ctnnnnccct	nnentaattn	ttctnnctan	540
ntcctanccn	cnnacnnncc	cancnatccn	nnnatacant	cnattntntn	cnntcncntn	600
cncnnttcc	nnctnnncnc	tncncatnc	ccnnnannan	canntncccc	ncctnccrna	660
ccnncnncnc	ccnccatccc	nnnccnnnt	ccnnantnga	caannnnaat	cncnnnnncn	720
nnnnnnnnnn	tnnnncccn	gcncnncnt	ncctcacnc	tnnnnnncta	nannnnntac	780
nnthaccnnt	cctnnacnc	tnccctnnng	antccnacna	ntnnnnnanc	nanaacnctn	840
tnnnnccata	atccacacc	acnccentnc	ancntntntt	ncntcntccc	ttcntatcnc	900
agctnnnnnt	nctntnnnnc	tncncccn	cnnactnchn	nnaccnchn	cccantcagt	960
ccacntccn	cnnnnnnntn	nnncnancn	ctnnacnncn	cnantaacct	ntnnncacct	1020
tccc						1024

<210> 47

<211> 236

<212> DNA

<213> E. Coli

<400> 47

atatacacta	agtgaatgat	atcttccgat	ttatcttaat	cgtttatgga	taacggcaaa	60
gggcttcggt	tttcctata	cttattcagc	actcacaat	aaaggaacgc	caatgaaaat	120
tatactctgg	gctgtattga	ttattttcct	gattgggcta	ctgggtgtga	ctggcgtatt	180
taagatgata	ttttaaatt	aattaatgtc	atcagggtccg	aaaataacga	gaatat	236

<210> 48

<211> 418

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(418)

<223> n = A, T, C or G

<400> 48

cggagattac	cgtgtgttgc	gatataat	ttagtctcgc	gtggcaatac	atcagtgcca	60
ataaaacgac	atatccagaa	aaatatacac	taagtgaatg	atatcttccg	attnatctta	120
ntcgtttatg	gataacggca	aagggtctcg	tttttctcta	tacttattca	gcactcacia	180
ataaaggaac	gccaatgaaa	attatactct	gggctgtatt	gattattttc	ctgattgggc	240
tactggtggt	gactggcgta	tttaagatga	tatttttaaaa	ttaattaatg	tcacaggtc	300
cgaaaataac	gagaataat	cagtctctca	tcctgttgcg	ctcctgtcat	gtgcattgct	360
tcatataatc	actggcgcaa	ggagcgcgca	ngggcgcgcc	aatcgccgcc	ggcccctg	418

<210> 49

<211> 550

<212> DNA

<213> E. Coli

<400> 49

ctgctagtta	cagggaacac	taatgacaga	cagctaaaag	ccctgtttaa	ttacgtatta	60
caaacagggg	atgccagcg	ttttcgtgca	tttattggtg	agatagcgga	acgcgcacca	120
caagaaaagg	agaaactgat	gaccattgct	gacagattac	gtgaagaagg	cgcaatgcag	180
ggcaaacacg	aagaagccct	gcgtattgct	caggagatgc	tgatagagg	tttagacaga	240
gagttagtta	tgatggtgac	ccgactttca	ccagacgatc	ttatcgcgca	aagccactaa	300

tcctgtaaca	cgggagtta	actggcggtat	gtttgctgta	aaccacatca	gcgaacgaca	360
tccgccagcg	cctcttctaa	atcgtagcag	cgaaacgcaa	aaccgccttc	ttccagccgt	420
ttaggcagcg	cgcgttgtcc	acctaatacc	agtactgaag	attcgcccat	taacagtcga	480
atggcggtcg	cggggacgcg	caaaatggcc	gggcgatgca	gcgcgatgacc	gagcgcatgg	540
gcaaattggt						550

<210> 50
 <211> 99
 <212> DNA
 <213> E. Coli

ttggcatctc	ggtgttgccg	atcttcatga	tatccagccc	gccggaaaact	tcttcccaaa	60
cggttttgct	gttatccatt	gagtcacgga	actgcccct			99

<210> 51
 <211> 259
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(259)
 <223> n = A,T,C or G

ccgtgccgag	atgatcctgt	naccatcatc	cgttgtgaag	tagtgattca	cgacttcaag	60
gcgcttttca	aaagggtatt	ttggctttga	catattaggg	gctattccat	ttcatcgncc	120
aacaaaatgg	gtgcagtaca	tactcnttgg	aatcaaacac	aggaggctgg	gaatgccgca	180
gaaatataga	ttactttctt	taatagtgat	ntgtttcacg	cttttatttt	tnaaanaagt	240
tnggcttact	tcccgggnn					259

<210> 52
 <211> 877
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(877)
 <223> n = A,T,C or G

cagcagagcg	cggccttctt	cgtagatgtt	cgcagtagtg	gtaatggtaa	tatccaaacc	60
acgaacgcgg	tcgactttat	cgtagtcgat	ttctgggaag	atgatctgct	cacggacacc	120
catgctgtag	ttaccacgac	cgtcgaaaga	cttagcggac	aggccacgga	agtcacggat	180
acgaggtaca	gcaatagtga	tcaggcgctc	aaagaactcc	cacatgcgtt	cgccacgcag	240
agttacttta	cagccgatcg	gatagccctg	acggattttg	aagcctgcaa	cagatttgcg	300
tgctttgggtg	atcagcggtt	tttgaccgga	gattgctgcc	aggtctgctg	ctgcgttatc	360
cagcagtttt	ttgtcagcga	tcgcttcacc	aacacccatg	ttcaggggtga	tcttctcgac	420
ccgagggact	tgcatgacag	aattgtagtt	aaactcagtc	atgagttttt	taactacttc	480
gtctttgtag	taatcatgca	gtttcgccat	cgtactactc	catgtcggtg	aacgctctcc	540
tgagtaggac	aaatccgccg	ggagcggatt	tgaacgttgc	gaagcaacgg	cccggagggt	600
ggcgggcagg	acgcccgcca	taaactgcca	ggcatcaa	taagcagaag	gccatcctga	660
cggatggcct	ttttgcgttt	ctacaaactc	ttttggttat	ttttctaaat	cattcaaata	720
tgtatccgnt	catcccatcc	tatcgatgat	aagctgtcaa	acatgagaat	ttaatcaatc	780
taaagtttta	tggngttaaa	cttgggctgg	cagnttncca	atggcttaat	cagtnagagg	840
ccctatntta	acgaactnng	ctantttngg	tcaatcn			877

<210> 53
 <211> 291

<212> DNA

<213> E. Coli

<400> 53

tgaacagcag	agatacggcc	agtgcggcca	atgttttttg	tcctttaaac	ataacagagt	60
cctttaagga	tatagaatag	gggtatagct	acgccagaat	atcgtatttg	attattgcta	120
gttttagtt	ttgcttaaaa	atattgttag	ttttattaaa	tgcaaaaacta	aattattggt	180
atcatgaatt	tgttgatga	tgaataaaat	ataggggggt	atagatagac	gtcattttca	240
tagggttata	aatgcgacta	ccatgaagtt	tttaattgaa	agtattgggt	t	291

<210> 54

<211> 282

<212> DNA

<213> E. Coli

<400> 54

ttattaaatg	caaaaactaaa	ttattggtat	catgaatttg	ttgtatgatg	aataaaatat	60
aggggggtat	agatagacgt	cattttcata	gggttataaa	tgcgactacc	atgaagtgtt	120
taattgaaag	tattgggttg	ctgataaatt	gagctgttct	attcttttta	aatatctata	180
taggtctgtt	aatggatttt	atttttacaa	ttttttgtgt	ttaggcata	aaaaatcaac	240
ccgcatatg	aacggcgggt	taaaatattt	acaacttagc	aa		282

<210> 55

<211> 293

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(293)

<223> n = A,T,C or G

<400> 55

cggggtccg	cgctcatcaa	caatcggggg	gcagcaagg	gctgaaacgg	gaaagcccct	60
cccgaagaag	gggccttgta	taaggaaagg	gttatgatga	agctcgctcat	catactgggt	120
gtgtngttac	tgtaaagttt	cccgaacttac	taacaactca	tcagaggggg	gagaaatcct	180
cccttaccct	tggtccctta	ctctagggtg	aaaaaacaac	agcgtcaata	ggcctgccat	240
gtacgaagcg	agatctgtga	accgctttcc	ggttagcctt	ttttatcctg	ttg	293

<210> 56

<211> 300

<212> DNA

<213> E. Coli

<400> 56

tctgcgttcc	gctaaaaggt	gcaaatgctc	aggacgttgc	agcgttttgc	gtgaccgctc	60
ggggaaggca	aaattgcctc	tgggaaagca	ttgcgcgggg	tccggcgctc	atcaacaatc	120
ggggggcagc	aaggggctga	aacgggaaag	cccctcccga	agaagggggc	ttgtataagg	180
aaagggttat	gatgaagctc	gtcatcatac	tggttggtgt	gttactgtta	agtttcccga	240
cttactaaca	actcatcaga	ggggggagaa	atcctccctt	acccttgctc	ctttactcta	300

<210> 57

<211> 359

<212> DNA

<213> E. Coli

<400> 57

caacacagga	ggctgggaat	gccgcagaaa	tatagattac	tttctttaat	agtgatttgt	60
ttcacgcttt	tatttttcac	ctggatgata	agagattcac	tgtgtgaatt	gcatattaaa	120
caggagagtt	atgagctggc	ggcgttttta	gcctgcaaat	tgaaagagta	agagtcttcg	180
gcgggaaatt	attcccgcct	tacttacggc	gttgcgcatt	ctcattgcac	ccaaatttat	240


```
tcttcacaaa aataataata gattttatta cgcgatcgat tatttatttc ctgaaaacaa 300
ataaaaaaat ccccgccaaa tggcagggat cttagattct gtgcttttaa gcagagatt 359
```

```
<210> 58
<211> 700
<212> DNA
<213> E. Coli
```

```
<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G
```

```
<400> 58
aaaccttttt ctctgtttt tcatagaggg caacccatgt cctgacctgg gttcggggga 60
caccaaaacg tgccgagatg atcctgtaac catcatcagt tgtgaagtag tgattcacga 120
cttcaaggcg cttttcaaaa gggatatttg gctttgacat attaggggct attccatttc 180
atcgtccaac aaaatgggtg cagtacatac tcggttgaaa tcaacacagg aggctgggaa 240
tgccgcagaa atatagatta ctttctttaa tagtgatttg ttccacgctt ttatttttca 300
cctggatgat aagagattca ctgtgtgaat tgcatttaa acaggagagt tatgagctgg 360
cggcgttttt agcctgcaaa ttgaaagagt aagagtcttc ggcgggaaat tattcccgcc 420
ttacttacgg cgttgccgat tctcattgca cccaaattta ttcttcacaa aaataataat 480
agattttatt acgcgatcga ttattttatt cctgaaaaca aataanaaaa tccccgcaa 540
atggcaggga tcttagattc tgtgctttta agcagagatt acaggctggg tacgttacca 600
gctgccgggc ctttaacgcc gctttcgatg gtgaaggaca ctttctgacc ttcgtccaga 660
gattgtaacc atcggctctg atagccnaga aatgtccaac 700
```

```
<210> 59
<211> 631
<212> DNA
<213> E. Coli
```

```
<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G
```

```
<400> 59
tggtggcatt ggttgctgga gagagaaaac cccgcacgt tgcaggtagt cacctgacaa 60
caccacgggg gctaattctt actctagacc actcaagaat agccgcgaaa cggtgtcatt 120
acaacacagg cggtatatg acgttcgcag agctgggcat ggcttcttgg catgatttag 180
cggctccggt cattgctggc attcttgcca gtatgatcgt gaactggctg aacaagcgga 240
agtaacgtgt catgcgggag tcaggctgcc gtaatggcaa tttgcgcccg gaccaggccg 300
caggggggaa actctgcggc ctttttcggt cttactgcgg gtaaggcacc cagtcgccgc 360
cggttcaggcg aacgtacggg ttatcctggt attgaataac tactgcattt gagttctcgg 420
agaccggtgc tggttggtgc aaccactgg tgagtttttt ccagtcaaca ttgtcttcgg 480
tgaaaatctt gccatcgaga acgcgaacca ccagatcgga gatagccagg aagctgctcg 540
gttggttcgat gacaatcggg gccccctgat gcgggtgcct catgccgaag aatttcaccc 600
caacggggac gtcngtgata gaccgggcta g 631
```

```
<210> 60
<211> 648
<212> DNA
<213> E. Coli
```

```
<220>
<221> misc_feature
<222> (1)...(648)
<223> n = A,T,C or G
```

```
<400> 60
```



```

ggctcaggcn tgctgattgt ttttttgtgc aatggcccng tattagcgtc gttgctgtcg      60
atggagagaa tcataaacgt ggtgaatgat gattgttagc aaggaaaact gtcaaaaatc      120
ttcaaaaaat ttgagggata aggccggaat ggctccggcc agagggaagt taaccgcgaa      180
gctgttgctg cttgagggtc gttttaacca gacgccaggc gtcctatcgc ccaaaaccgc      240
gtctggccca gcggaaccag atattaggat ggcgaaatcgt ccagatcgcc atcacgtac      300
tgccaaccag cgccaggag cgacactta gcagcatatt ccancgacga tcgtaagcgc      360
ctgttgcttc cagccattca cgacgactgg cggaaggngc cgcnctgac caacttgnct      420
tttagnctga tncanattan attnataaac gcagnanncn ggtntgatta atcntatttn      480
gctctngtct ggtagttagc nncggnnngt ctenttntna ccennttcnn tttannttac      540
natnngtaan ttatnttnt nngtctnant tntanttgng tactntaagt ntatncgnnn      600
atnntnnnan nnnncagunc ntntttttta aatntttnt nanncnnc      648

```

<210> 61

<211> 737

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(737)

<223> n = A,T,C or G

<400> 61

```

tgctaataac tttctcattg agatgaaaat taaggttaagc gaggaaacac accacacccat      60
aaacggaggc aaataatgct gggtaatatg aatgttttta tggccgtact gggaataatt      120
ttattttctg gttttctggc cgcgtatttc agccacaaat gggatgacta atgaacggag      180
ataatccctc acctaacggc ccccttgcta cagttgtgta caaggggcct gatttttatg      240
acggcgaaaa aaaaccgcca gtaaacgggc ggtgaatgct tgcattggata gatttgtgtt      300
ttgcttttac gtaaacaggc attttcctgc actgataacg aatcgttgac acagtagcat      360
cagttttctc aatgaatggt aaacggagct taaactcggc taatcacatt ttgttcgtca      420
ataaacatgc agcgatttct tccggtttgc ttaccctcat acattgcccg gtccgctctt      480
ccaatgacca catccagagg ctcttcagga aatgcgcgac tcacacctgc tgtcacggta      540
atgttgatat gcccttcaga atgtgtgatg gcattggtat cgactaactg gcaaattctg      600
acacctgcac gacatgcttc ttcattcatta gccgcttga caataatgat aaattcttcg      660
cccccgtagc gataaacctg ttcgtaatna cgcgtccaac tgggntaagt aaagtgtcca      720
gggtgccgta atcttac      737

```

<210> 62

<211> 648

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(648)

<223> n = A,T,C or G

<400> 62

```

tgcttttgaa tatgtgctcg caatcttgag aaggaaatgg cgaccacgaa agaaaaggca      60
aaaaccgata atctgaaaga acccaagtat ttcagtataa gcattgaatg ccgaccagta      120
aactctttcg gattcaccca gaaagtgaan ccaaaatgat aatcgtatac ataagtcttt      180
cgagtggctc gttagcaaaa agtttcaaca atggagtaaa tacatccaac atatcaataa      240
ctctcaactg taaggggatt gaaatggtaa ccccgactct tcgcttgagg ggtatagccg      300
agaccaccga agccccggag gtgggtgaaat aaaaccgggc acaacacgaa agggcgcat      360
tccgatatcc ataaaagaag tccgggtctt gtctggtaaa attaaattgg tgggaagtgc      420
gcctccgggt tgtaaatacc gactttgctg ggtgtagcct ggccgcatca agtttttttc      480
tggaagttcg ctgatgtccg ccctttttta agggaaattt ggtgatgccg gtgaatgccg      540
cttaaccccc cgtgggcccc gttaaaagtc atggttaagc ctaatnggtt tgggggtggga      600
aaagccnact gnaaattggt tacctggttt gcaagtancg ctggaagg      648

```

<210> 63

<211> 237
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(237)
 <223> n = A,T,C or G

<400> 63
 ggtgtttant tacaagagat tcatctttgt ntaaancccn gataagtaat tacgcataaa 60
 acaacaatga ttataatagc aaaaataaat attatcatct ttgatagatt acttgagata 120
 gccagcatct tgtaaagcct ttatcgtttt tttatgctct ggattaatat aatcactaca 180
 tctatctgag caatctgttg ttgatggaca tgtcaacca tggtcattta cagccaa 237

<210> 64
 <211> 427
 <212> DNA
 <213> E. Coli

<400> 64
 gataattaga gtttgcctgc agaaaattga cgttacccat acaaatgaa aggccaggta 60
 aatcatgcca ttagtcattg ttgctatcgg tgtaatcttg ttgttgctcc tgatgatccg 120
 cttcaaaatg aacggcttca tcgctctcgt cctcgtggcg cttgctgttg gattaatgca 180
 aggaatgccg ctggataaag ttattggctc catcaaagcc ggtgtcggcg ggacgctcgg 240
 tagccttgcc ctgacatagg gttttggcgc aatgctgggc aaaatgctgg cagactgcgg 300
 tggcgcacaa cgtatcgcca ccacgctgat tgccaaattt ggtaaaaaac acatccagt 360
 ggcggtggtg ctgaccggtt ttaccgttgg ttttgccctg ttctatgaag tgggctttgt 420
 gctgatg 427

<210> 65
 <211> 261
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(261)
 <223> n = A,T,C or G

<400> 65
 caaagaacct tcaacatgaa aaatatccat ttgtttgcaa aaaaagatta ttaggaagga 60
 aattaatgca attatcgaaa attcaaaaaa tatccaaaaa tngtatactt tattccagaa 120
 gagttcaata taatgtttgt cttcaatttt tcttacttca gggtaatata gattgctcat 180
 tacattgtga gcttcatctt tatttaattt tctgttgact ccagctctcc gtgataacgg 240
 ttttataatt agatgcttat c 261

<210> 66
 <211> 98
 <212> DNA
 <213> E. Coli

<400> 66
 agatgattgc cgggaacttg ttagcggcac gcaggcggcg gctcgcaccc ttaccctgct 60
 ctttacgtac ttctgcgttg atagtaaaca tttctttc 98

<210> 67
 <211> 260
 <212> DNA
 <213> E. Coli

<400> 67
aagcgcgaac gaagtcgatg tgctgcagct tcggtttcta cgggtgacgc tgtacgtcct 60
gagctttaac ttgtatttct ttaccgtcaa caacgatggc cagaacttcg ctgtagaatt 120
cagctttagc ttgcatgttc atgactttgt cgtgatccag ctcgatagcc agcggcgctt 180
ctttgccacc gtagatgatt gccgggaact tgtttagcgc acgcaggcgc cggctcgcac 240
ccttaccctg ctctttacgt 260

<210> 68
<211> 95
<212> DNA
<213> E. Coli

<400> 68
aaaaacggcg taaagaaagg ttgcaaacat gtttaataaaa actcaaattg atcccacgta 60
tatattacgc cgcaaaatcc ttacaataaa caggg 95

<210> 69
<211> 174
<212> DNA
<213> E. Coli

<400> 69
ttaattatta aaatagtcta acgcgattat gtgggttatgg gggtaaacat taaataaacc 60
agcggggagg ggaggtaaag tgaaaaaata aaaagcggat aatcttaata agcaggccgcg 120
acagcatcgc catccggcac tgatacgagg tttatttcag ctcatcaacc atcg 174

<210> 70
<211> 138
<212> DNA
<213> E. Coli

<400> 70
agtctgtaaa aacgtcaaaa agagtgtttt atcaacagaa gaatggaggt ctgacagata 60
gtagtaatgc aaaaaaatgg agacttaagt tgaatgaacg ggagtaaagc gaaaagacta 120
tagagtgaag gagaaatt 138

<210> 71
<211> 191
<212> DNA
<213> E. Coli

<400> 71
tttgttggtc taatattcta ttgttatctt tatttataga tgtttatatt gcatgaggtg 60
gtttttggag agaagaatga ggaagatgcg tcgagccaca gaaacgttag ctttacatat 120
agcggaggtg atgtgaattt aatttacaat agaaataatt tacatatcaa acagttagat 180
gctttttgtc g 191

<210> 72
<211> 244
<212> DNA
<213> E. Coli

<400> 72
ggccatttat acaggaaaaag cctatgtcag aacgtaaaaa ctcaaaatca cgccgtaatt 60
atctcgtaa atgttcctgc ccaaactgca cccaagagtc agaacacagt ttttcaagag 120
tacaaaaagg tgcccttttg atctgccctc attgcaacaa agtattccag acaaattcta 180
aagctgtagc ctgattgatt ttattagtaa caagtatttt ttatatttta ataatatatt 240
taaa 244

<210> 73
<211> 327

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(327)

<223> n = A,T,C or G

<400> 73

aaattttcag gtaccttgtc accatacttt tttttctgag cattaatgat attttgagct	60
tcttgaggat ctttaactcc ccacatttgg tggaaagtat tcatattaaa aggaaggntg	120
aataatttgn ctttataaat cgccagtgga gaattagtaa aacgattaaa ttctactaaa	180
tnattaaccg naaaaaaatt cccatatata tttatcattg gtatgaaaaa tatgtgcacc	240
atatttatga atntggatac cctnacagtc ctctgtgtac gcatttccac cgatatgatt	300
tcttttctna atcactaaaa ctttttt	327

<210> 74

<211> 150

<212> DNA

<213> E. Coli

<400> 74

gcagtgatcg aagcgatgac gaagtgtatg gaaaaatcag aaaaactcag caaatcctga	60
tgactttcgc cggacgtcag gccgccactt cgggtgcggtt acgtccggct ttctttgctt	120
tgtaaagcgc caaatctgcc gatttcaacc	150

<210> 75

<211> 330

<212> DNA

<213> E. Coli

<400> 75

gaaagtatct tcgttattga catcactgga aaatataact tgcttttcat tattaactc	60
gaagcgcgta ccgtatctgg acaaacattt atcgagctta ccaaattcct gaagaggttt	120
aactacagat aacatttgcg cgtcctttgc agtaatgcc gtcaaactct tgacgggcat	180
tatttagatt aaattaccag tatttcttcg gagtgaagaa tattaccagg tatatttaac	240
accacggtc gcggaccagt cttgatctac gtcaccacca ccgaggtagt tagcatcggt	300
ataggcgcgtg aagtctcttg tgaagctaaa	330

<210> 76

<211> 194

<212> DNA

<213> E. Coli

<400> 76

tgtttttttc cagcaacgga gcaaaagggt tggccttgtg cagctcaggg ttaaccactt	60
taactacgtg gcgacgaccc ggagatgtcg gtttacattt aacaactgcc attgtattac	120
tctccgact tactcagcgc cgccaacgaa gtccagattc tggccttctt tcagggtgac	180
gtaagctttt ttcc	194

<210> 77

<211> 188

<212> DNA

<213> E. Coli

<400> 77

tccctttaac taccagggtg ttaacgactt cgacttcgac ttcaaacagt ttctgcacag	60
cagctttgat ttctgctttg gtcgcgtctt tagcaacttt gactactatg gtgttggtt	120
tttccatcgc agtagacgct ttttcagaaa cgtgcggtgc acgcagcacc ttcagcagac	180
gttcttca	188

<210> 78
 <211> 173
 <212> DNA
 <213> E. Coli

<400> 78
 acaaaggcga acaaagcctg tgaagcccga aggctccaca gacagtgccta cttgaaggcc 60
 ttactgtttc ttcttaggag cgagcaccat gatcatctgg cggccttcga tcttggttgg 120
 gaaggattcg accactgccg gttcttgcaa atcgtctttc acgcgattaa gca 173

<210> 79
 <211> 272
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(272)
 <223> n = A,T,C or G

<400> 79
 tggagaaaac ggggtattga taaagcaatc atcgttctag gggcggttaat tgcgctgctg 60
 gaactgatcc cgctttctgc ttcaagcttc tgaactggat acggaaacgt aatnagggct 120
 aaagaagaca ctactcttag ccctttaaca tttaacgcat tgtcacgaac tcttctgccg 180
 ccgttggttg aatggcgacg ggtattggtc gaaatctttt ttgggtggcc ccatctttaa 240
 cgcccacccg cgaaaccctg caacatttcg tc 272

<210> 80
 <211> 259
 <212> DNA
 <213> E. Coli

<400> 80
 cgcaggcagc tgatgggtcaa caggatgaga gaaaccaga gacagggttaa tcacattgcc 60
 tttaacgcgt gcacggtaac ctacaccaac cagctgcagc ttcttagtga agccttcggt 120
 aacaccgata accattgagt tcagcagggc acgcgcggta ccagcctgtg cccaaccgtc 180
 tgcgtaacca tcacgcggac cgaaggtcag ggtattatct gcatgtttaa cttcaacagc 240
 atcgttgaga gtacgagtc 259

<210> 81
 <211> 73
 <212> DNA
 <213> E. Coli

<400> 81
 caggtcggaa cttacccgac aaggaatttc gctaccttag gaccgttata gttacggccg 60
 ccgtttaccg ggg 73

<210> 82
 <211> 666
 <212> DNA
 <213> E. Coli

<400> 82
 atgaacgttt tctcgcaaac tcaacgctat aaggcgttgt tctggttato gttatttcat 60
 ctgctggtga tcacctccag taactatctg gttcagcttc ccgtctccat tttgggttcc 120
 cataccacct ggggcgcgtt tagctttccg tttatttttc ttgctaccga cctgaccgtg 180
 cgtatttttg gcgcaccgct ggcccgaacg attatcttcg cggtaatgat cctgcggtta 240
 ttaatctcct acgtcatctc gtcgctatcc tatatgggtt cctggcaggg attcggcgca 300
 ctcgcccact tcaacctgtt tgcgcccgt atcgccaccg ccagtttcat ggcttacgag 360
 ctggggcaaa tcctcgacgt gcacgttttt aaccgcctgc gtcagagtcg ccgctggtgg 420

ctggcaccga	cagcgtccac	actgttcggt	aacgtcagcg	acacgctggc	ctttttcttc	480
attgccttct	ggcgtagccc	ggatgccttt	atggctgaac	actggatgga	aatcgcgctg	540
gtcgattact	gtttcaaagt	gttaatcagt	atcgttttct	tcctgccaat	gtatggcgta	600
ttactcaata	tgctgttgaa	aagactggca	gataaatccg	aaatcaacgc	tttgaggcg	660
agttaa						666

<210> 83
 <211> 612
 <212> DNA
 <213> E. Coli

<400> 83						
gtgataagat	ggatgaatga	gccgttatgg	ccgtttatcg	aaaggaagaa	gtcaatgcgc	60
aatctgggta	aatatgtcgg	aattggcctg	ctggttatgg	ggcttgccggc	ctgtgatgat	120
aaagacacta	acgctacggc	gcagggttcg	gtcgcggaaa	gtaacgctac	cggaatccc	180
gtcaacctgc	ttgatggcaa	gttaagtctc	tcgctgccag	cggatatgac	cgaccagagc	240
ggtaagctgg	gaacgcaggc	caataacatg	catgtctggt	ccgacgccac	cgggcagaaa	300
gcagtcacgc	tcacatggg	cgatgatccg	aaagaagatc	tggcggtgct	ggcgaagcgt	360
ctggaagatc	agcaacgtag	ccgcgatccg	cagctgcaag	tggttaaccaa	taaagccatt	420
gagctgaaag	gtcacaaaat	gcagcagtta	gacagtatta	tctccgcgaa	aggccagacg	480
gcgtactctt	ccgttattct	gggtaacgtg	ggtaatcaac	tgctgaccat	gcaaattacg	540
ctgcccgcgtg	acgatcagca	aaaagcgcag	accaccgcag	aaaacatcat	taatacgcgtg	600
gttattcagt	aa					612

<210> 84
 <211> 975
 <212> DNA
 <213> E. Coli

<400> 84						
atggcgaata	tgtttgccct	gattctgggtg	attgccacac	tggtgacggg	cattttatgg	60
tgctgtggata	aattcttttt	cgcacctaaa	cggcgggaac	gtcaggcagc	ggcgaggcg	120
gctgccgggg	actcactgga	taaagcaacg	ttgaaaaagg	ttgcgccgaa	gcctggctgg	180
ctggaaaccg	gtgcttctgt	ttttccggta	ctggctatcg	tattgattgt	gcgttcgctt	240
atttatgaac	cgttccagat	cccgtcaggt	tcgatgatgc	cgactctgtt	aattggtgat	300
tttattctgg	tagagaagtt	tgcttatggc	attaaagatc	ctatctacca	gaaaacgcgtg	360
atcgaaaccg	gtcatccgaa	acgcggcgat	atcgtggtct	ttaaatatcc	ggaagatcca	420
aagctttgatt	acatcaagcg	cgcggtgggt	ttaccgggcg	ataaagtcac	ttacgatccg	480
gtctcaaaag	agctgacgat	tcaaccggga	tgcatgtccg	gccaggcggtg	tgaaaacgcg	540
ctgccgggtca	cctactcaaa	cgtggaaccg	agcgatttctg	ttcagacctt	ctcacgccgt	600
aatggtgggg	aagcgaccag	cggattcttt	gaagtgccga	aaaacgaaac	caaagaaaat	660
ggaattcgtc	tttccgagcg	taaagagaca	ctgggtgatg	tgacgcaccg	cattctgaca	720
gtgccgattg	cgcaggatca	ggtggggatg	tattaccagc	agccagggca	acaactggca	780
acctggattg	ttcctccggg	acaatacttc	atgatgggcg	acaaccgcga	caacagcgcg	840
gacagccgtt	actggggctt	tgtgccggaa	gcgaatctgg	tcggtcgggc	aacggctatc	900
tggtatgagct	tcgataagca	agaaggcgaa	tgcccgaactg	gtctgcgctt	aagtcgcatt	960
ggcgccatcc	attaa					975

<210> 85
 <211> 1761
 <212> DNA
 <213> E. Coli

<400> 85						
ttgaccatta	cgaaacttgc	atggcgtgac	ctggttcctg	ataccgatag	ctatcaggaa	60
atattttgctc	agccacattt	gattgacgaa	aacgatcctt	tattcagtga	tactcaaccg	120
cggtctgaat	ttgcgctgga	gcagttgctg	catacgcgag	catcctcctc	ttttatgctg	180
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 <211> 1185
 <212> DNA
 <213> E. Coli

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<210> 87
 <211> 2115
 <212> DNA
 <213> E. Coli

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<210> 88

<211> 540

<212> DNA

<213> E. Coli

<400> 88

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<210> 89

<211> 1549

<212> DNA

<213> E. Coli

<400> 89

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<210> 90

<211> 375

<212> DNA

<213> E. Coli

<400> 90

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<210> 91

<211> 366

<212> DNA

<213> E. Coli

<400> 91

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<210> 92

<211> 498

<212> DNA

<213> E. Coli

<400> 92

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<210> 93
 <211> 2145
 <212> DNA
 <213> E. Coli

<400> 93

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<210> 94
 <211> 1767
 <212> DNA
 <213> E. Coli

<400> 94

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<210> 95
 <211> 1227
 <212> DNA
 <213> E. Coli

<400> 95						
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<210> 96
 <211> 900
 <212> DNA
 <213> E. Coli

<400> 96						
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<210> 97

<211> 771

<212> DNA

<213> E. Coli

<400> 97

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<210> 98

<211> 1335

<212> DNA

<213> E. Coli

<400> 98

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<210> 99
 <211> 1536
 <212> DNA
 <213> E. Coli

<400> 99

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<210> 100
 <211> 1029
 <212> DNA
 <213> E. Coli

<400> 100

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<210> 101
 <211> 993

<212> DNA

<213> E. Coli

<400> 101

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<210> 102

<211> 1023

<212> DNA

<213> E. Coli

<400> 102

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<210> 103

<211> 876

<212> DNA

<213> E. Coli

<400> 103

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<210> 104

<211> 291

<212> DNA

<213> E. Coli

<400> 104

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<210> 105

<211> 1152

<212> DNA

<213> E. Coli

<400> 105

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<210> 106

<211> 3048

<212> DNA

<213> E. Coli

<400> 106

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<210> 107

<211> 885

<212> DNA

<213> E. Coli

<400> 107

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<210> 108

<211> 654

<212> DNA

<213> E. Coli

<400> 108

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cagtacttcc	cgatgcagg	tggtcgctac	agcctgctga	tccacgcggc	tgcggtgac	480
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aaagggatga	tcgaaggga	ggtaagtcgt	cgctgggcga	agaaacacca	tccgcgctgg	600
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<210> 109

<211> 261

<212> DNA

<213> E. Coli

<400> 109

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tcgtagggc	actacgagac	accaacctgc	cagaagggtg	gcccgatccc	caatactatt	180
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<210> 110

<211> 1203

<212> DNA

<213> E. Coli

<400> 110

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taa

1203

<210> 111
 <211> 1179
 <212> DNA
 <213> E. Coli

<400> 111

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<210> 112
 <211> 1326
 <212> DNA
 <213> E. Coli

<400> 112

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<210> 113
 <211> 585

<212> DNA

<213> E. Coli

<400> 113

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aacattgcgc	aactgggtta	cgacgaagac	gaagatcagg	aagagcttga	aatgtcgcgt	480
gaagagatca	tcgaatacgt	tcgtgttgcc	gcgtgttat	gccacgacac	ctttactcat	540
ccgcaaccga	ccgcgccaga	agtacaaaaa	ccgactctac	actaa		585

<210> 114

<211> 363

<212> DNA

<213> E. Coli

<400> 114

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gtggtttttg	gtggtttgtat	ctatgtcgcg	catacaaacc	aagctcttgc	aaacttcgca	120
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gccatcagcc	tgggtgtcgg	tttcgtctat	tcaaagttca	ttgtctttag	ggatgcgaaa	360
tga						363

<210> 115

<211> 921

<212> DNA

<213> E. Coli

<400> 115

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<210> 116

<211> 1332

<212> DNA

<213> E. Coli

<400> 116

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<210> 117

<211> 249

<212> DNA

<213> E. Coli

<400> 117

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gtagtcggcg	gatggatcag	cacgctgttt	ggctttggta	aagtcgatgg	cttcaatttt	180
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aaaagttaa						249

<210> 118

<211> 183

<212> DNA

<213> E. Coli

<400> 118

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taa						183

<210> 119

<211> 360

<212> DNA

<213> E. Coli

<400> 119

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aagtggcaca	acattgaagc	catgactgac	gatacttatt	tcaacattga	cttcttcgtg	300
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<210> 120

<211> 741

<212> DNA

<213> E. Coli

<400> 120

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<210> 121

<211> 1395

<212> DNA

<213> E. Coli

<400> 121

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<210> 122

<211> 3123

<212> DNA

<213> E. Coli

<400> 122

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<210> 123

<211> 3078

<212> DNA

<213> E. Coli

<400> 123

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<210> 124

<211> 1416

<212> DNA

<213> E. Coli

<400> 124

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<210> 125

<211> 1035

<212> DNA

<213> E. Coli

<400> 125

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gttgccggcg	agtcaaaact	tacagataca	acggtttcaa	ttccgataac	agccagttac	960
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<210> 126

<211> 2481

<212> DNA

<213> E. Coli

<400> 126

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gttgcaaata	ttcgtcttga	tgataatcaa	cccttaccgg	ggcagtatga	catcgatatt	180
tatgtcaata	agcaatggcg	cgggaaatat	gagattattg	ttaaagacaa	cccgaagaa	240
acatgtttat	caagagaagt	tatcaagcgg	ttaggcatta	atagcgataa	cttcgccagc	300
ggtaagcaat	gtttaacatt	tgagcaactt	gttcagggtg	ggagctatac	ctgggatatc	360
ggggtttttc	gtctcgattt	cagtgtcccg	caggcctggg	tggagaact	ggaaagtggc	420
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<210> 127

<211> 720

<212> DNA

<213> E. Coli

<400> 127

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cgcattattt	atccggcaga	aaataaagaa	gtgatgggtc	agttgatgaa	ccagggaacc	180
cgttcttcgc	tgctgcaggc	gtggattgat	gatggcgata	cgctattacc	accagaaaaa	240
attcagggtt	ctttcatggt	aacgccacca	gtggcaaaaa	taggggcaaa	ttccggggcag	300
caagtaaaaa	tcaaaattat	gccgaataaa	ctgcccacta	ataaagaaag	cattttttat	360
ctgaatgttc	tggatatctc	accaaatagt	ccagagcaag	aaggtaagaa	tgcactgaag	420
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gactcagcta	attgggtgac	gatttcggat	gtcaaaagct	ataatgtcaa	agtcaattat	600
gaaactatta	tgattgcccc	cttagaaagt	cagagtgtta	atgtcaaaa	taataatgca	660
aataactggc	atctgaccat	tatcgatgac	catggcaact	atattagtga	caaaatttaa	720

<210> 128

<211> 543

<212> DNA

<213> E. Coli

<400> 128

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tgtaaatctg	aagcgggtgg	tgattcagta	agtattaata	tgccgactgt	accaaccagt	180
gtctttgaag	gtaaagctaa	atattctacc	tatgatgatg	cagtcgggtg	aaccagcagc	240
atgttaaaaa	ttagctgccc	gaaagaagtt	gctggtgtaa	aactctcggt	gattaccaac	300
gataaaataa	ccggtaacga	taaggcgata	gccagtagca	acgataccgt	gggttactat	360
ctctatttag	gtgataacag	cgatgtcctg	gatgtttctg	caccttttaa	cattgagagt	420
tataaaacag	cggaaggtca	atatgctatt	ccgttttaag	caaaataacct	gaaactgaca	480
gataactcag	tgcaatcagg	tgatgtgtta	tcttctctgg	ttatgcgtgt	ggcgcaggat	540

taa

543

<210> 129
 <211> 339
 <212> DNA
 <213> E. Coli

<400> 129
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 agctttggct ttccagtaat tcttgctcga ggagcaattt tactgacagg gatagtgtgt 180
 acagttgttt taaatgaaat cgatgctcaa tgccatttat cagaaaaatt aaaatatgca 240
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 ccatttatgt atgttcttaa cactccaccc gtgatatga 339

<210> 130
 <211> 582
 <212> DNA
 <213> E. Coli

<400> 130
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 gctgtcgggt tctcgtcggg gatggtgctc ttcgccgcca tccgcgaacg ccttgcgtgtg 480
 gctgatgtcc cggcaccttt tcgcggtaat gccattgcgt taattaccgc aggtcttatg 540
 tctctggcct ttatgggctt tagtggtttg gtgaagttgt aa 582

<210> 131
 <211> 579
 <212> DNA
 <213> E. Coli

<400> 131
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 gacgaaatct taccgcagag ccagtgtggt cagtgcggtt atcccggtg tcgcccctac 180
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 gtgatgctaa aaattgccga gttgcttaat gtcgagccgc agccgctgga tggcgaagcg 300
 caagagataa cgctgcgcg gatggtggcg gttattgatg aaaataactg tattggctgc 360
 actaaatgta ttcaggcgtg tccggtagac gccatcgttg gcgctaccgc tgccatgcat 420
 acggtaatga gtgatctctg tacgggctgc aatttatgtg ttgatccgtg cccgacgcac 480
 tgcattctctg tgcaaccggt cgcagaaaca cctgactcct ggaaatggga tctgaacacc 540
 attcccgtgc gtatcattcc cgtggaacac catgcttaa 579

<210> 132
 <211> 2223
 <212> DNA
 <213> E. Coli

<400> 132
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 catccaccgg agatgaaaaa ccagtccaac ggtacacccc tgcgccagg accctggcg 120
 cagcgttttg ttattccact gaaacagcat attggcgctg aaggtagatt gtgcgttagc 180
 gtcggcgata aagtattgcg cggccagccg ctacccgtg gtcgcgga aatgctgct 240
 gttcacgcgc ccacctcggg taccgttacg gctattgcgc cccactctac ggctcatcct 300
 tcagctttag ctgaattaag cgtgattatt gatgccgatg gtgaagactg ctggatcccc 360

cgcgacggct	gggcccgatta	tcgcactcgc	agtcgcgaag	agttaatcga	gcgcatacat	420
cagtttggtg	ttgccgggct	gggcccgtgca	ggattcccga	caggcggttaa	attgcagggt	480
ggcggagata	agattgaaac	gttgattatc	aacgcggctg	agtgcgagcc	gtacattacc	540
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cagcaacagg	ctaattgcggt	accagaagaa	caggttgatc	cgcgcaaagc	ggcagttgcc	2160
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<210> 133

<211> 1059

<212> DNA

<213> E. Coli

<400> 133

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tggggctactc	tcgttcagat	cctgttggca	tcggttagtg	ctctgttagc	cgaagctctc	180
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acaggcttat	tgctggcgg	aagtattccc	cccctcgcgc	catgggtggat	ggctgtgctg	300
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cctgacggcg	tggtcttttc	cgtcctgctg	cggaacatca	cggttccctc	gatcgattac	1020
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<210> 134

<211> 621

<212> DNA

<213> E. Coli

<400> 134

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gggttaactg	cgccatcaa	ccagatgacc	aaaacgacga	ttgctgaaca	ggccagtctg	120
caacaaaagg	cgttatttga	tcaggtgctg	ccagccgaac	gctataacaa	tgcgctggca	180
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aagaaagatg	gtggtgattt	cgaccagttc	accggcgcgga	cgattactcc	ccgcgcgggtg	540
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<210> 135

<211> 696

<212> DNA

<213> E. Coli

<400> 135

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gcaggaaaat	acctgattga	tgaagaatg	aaaaagcgcc	gtgctgaagc	agctgcagaa	660
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<210> 136

<211> 636

<212> DNA

<213> E. Coli

<400> 136

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caggcgaccg	atgtcagtg	taataaggcg	acggcgaaac	tctaccgggt	ggcgaaatag	180
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<210> 137

<211> 504

<212> DNA

<213> E. Coli

<400> 137

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<210> 138

<211> 531

<212> DNA

<213> E. Coli

<400> 138

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<210> 139

<211> 1149

<212> DNA

<213> E. Coli

<400> 139

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<211> 417

<212> DNA

<213> E. Coli

<400> 140

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<211> 186

<212> DNA

<213> E. Coli

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<211> 1197

<212> DNA

<213> E. Coli

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<210> 145

<211> 291

<212> DNA

<213> E. Coli

<400> 145

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ttcttacctg	attattcccc	catgaatcgt	gattcctttt	atccagccat	cgctgtttt	120
ccgctgttac	tgatgctggc	cggtgtgctg	cctatgcatg	aaacccgcca	ggcgttaagc	180
cagcaaagc	ccgctgcaca	agttgacacc	gcattaccca	cgcgctgaa	aatggttggc	240
cagacagcca	atggtggctg	gagtatcacg	ataatcaact	cacttcctta	a	291

<210> 146

<211> 948

<212> DNA

<213> E. Coli

<400> 146

atgctgtgtg	tactggcacc	gatggaggga	gtgcttgact	ctctggtgcg	tgaattgctg	60
accgaagtta	acgactacga	tctgtgcac	accgagtttg	tccgctgggt	ggatcaactg	120
ctgccggtaa	aagtctttca	tcgcatttgc	cctgagctac	aaaacgccag	ccggacacca	180
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caggggtgaa	aagcgatgct	tgaagctgta	ccggcgcat	tgcccgtcag	cgtgaaagtg	420
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gaaccgcaa	tgccgtggcc	ggaggtggtt	gctttgctgc	aaaaatatac	ccgtctggaa	780
aagcagggcg	ataccgggtt	atatcacgtt	gcgcggatta	aacagtggtt	gagttatttg	840
cgtaagaat	acgatgaagc	aacggaatta	tttcagcatg	ttcggtgtt	gaataattcc	900
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<210> 147

<211> 891

<212> DNA

<213> E. Coli

<400> 147

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ccagacaccg	cgcggtattt	tattgatatt	catcttcccg	cgccgctgcg	caaactgtgt	120
gatttaacga	cgcttaaaact	ggaaccaaac	agttttattg	atgaagacct	gcggcaatat	180
tattccgacc	tcttgtggtc	tgtgaaaacg	caggaggag	tgggttatat	ttatgtagt	240
atagagcacc	aaagtaagcc	ggaagaatta	atggcttttc	gcatgatgct	ttattccatt	300
gcggcaatgc	aaaaccatct	tgatgcgggc	tataaagagc	ttccattggt	gctcccgatg	360
ctgttttatc	atggttgacg	aagtccttat	ccttattcac	tctgctggct	tgatgaattt	420
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gtggtgcccg	atgacgagat	tatgcaacac	cgcaaatggt	cgctgttgga	gttaattcag	540
aaacatatcc	gtcagcgcca	tctgttgga	ttagtcgacc	aaattgtttc	gctgctagtt	600
acaggaaca	ctaagacag	acagctaaaa	gccctgttta	attacgtatt	acaaacagg	660
gatgcccagc	gttttcgtgc	atattattggt	gagatagcgg	aacgcgcacc	acaagaaaag	720
gagaaactga	tgaccattgc	tgacagatta	cgtgaagaag	gcgcaatgca	gggcaaacac	780
gaagaagccc	tgctgattgc	tcaggagatg	ctggatagag	gttttagacag	agagttagtt	840
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<210> 148

<211> 1668

<212> DNA

<213> E. Coli

<400> 148

gtggctcaat	tcgtttatatac	catgcatcgt	gtcggcaaag	ttgttccgcc	gaaacgtcat	60
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aacccggaac	acaccgtgcg	tgagtccatt	gaagaagcgg	tttcagaagt	ggttaacgcc	300
ctgaaacgcc	tgatgaagt	gtatgcgctg	tacgccgac	cggatgccga	ttttgacaag	360
ctggccgctg	aacaaggccg	tctggaagag	atcattcagg	ctcacgacgg	tcataatctg	420
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gttggcgcca	acatgctgct	gctcgacgaa	ccaaccaacg	acctggatat	cgaaccctg	1440
cgcgcgctgg	aaaacgcctt	gctggagtgc	ccgggctgtg	cgatggttat	ctcgcacgac	1500
cgttggttcc	tcgaccgtat	cgcacgcac	attctggatt	accaggatga	aggtaaagtt	1560
gagttcttcg	aaggtaactt	taccgagtac	gaagagtaca	agaaacgcac	gctgggcgca	1620
gacgcgctgg	agccgaagcg	tatcaagtac	aagcgtattg	cgaagtaa		1668

<210> 149

<211> 522

<212> DNA

<213> E. Coli

<400> 149

atgtcaaagc	caaaataccc	ttttgaaaag	cgccttgaag	tcgtgaatca	ctacttcaca	60
actgatgatg	gttacaggat	catctcggca	cgttttggtg	tccccgaac	ccaggtcagg	120
acatgggttg	ccctctatga	aaaacatgga	gaaaaagggt	taattcccaa	acctaaggc	180
gttagtgctg	atccagagtt	gcgtattaag	gtcgtgaaag	ctgtgatcga	gcagcacatg	240
tcctttaatc	aggctgctgc	tcactttatg	cttgctggta	gtggttctgt	agccagggtg	300
ctgaaggtct	atgaagagcg	cggagaagct	ggtttacgcg	cgctcaagat	tggcacaaaa	360
agaaacattg	caatatcagt	tgatccagaa	aaagcggcat	cagcattgga	gctgtcaaaa	420
gaccgacgca	ttgaggatct	tgaaaggcaa	gttcgatttc	ttgaaacgcg	gcttatgtat	480
ctaaaaaagc	tgaaagcctt	agctcatccc	acgaaaaagt	ga		522

<210> 150

<211> 852

<212> DNA

<213> E. Coli

<400> 150

gtgaaagtac	tcaacgagct	aaggcagttt	tatcctcttg	atgagcttct	cagggctgcg	60
gagataccgc	gcagtagctt	ttattatcat	ctaaaggctc	tcagcaagcc	tgacaagtat	120
gcggacgtta	aaaagcgtat	tagtgagatt	tatcacgaga	atagaggccg	atacggatac	180
cgtagggtaa	cgctgtctct	tcacgagaa	gggaaacaga	ttaccataa	agctgttcag	240
cgcctgatgg	gaacctctc	acttaaagca	gcgattaagg	tcaagcgata	ccgctcttac	300
agaggagagg	tagggcaaac	cgccttaaat	gttctccaaa	gagatttcaa	ggctacgcgg	360
ccaaacgaga	agtgggttac	cgatgttact	gaatttgacg	tcaatgggcg	caagctgtat	420
ttgtctccag	taatagatct	cttcaacaac	gaagttatct	cttacagcct	ttcgaaaga	480
ccagtgatga	acatggttga	gaatatgctc	gatcaggcat	tcaaaaagct	taatcctcac	540
gagcatcctg	ttctgcactc	tgaccaggga	tggcagttat	gtatgagaag	atatcaaaat	600

atccttaaag	aacatggtat	taaacaaagc	atgtccagaa	aaggcaattg	tctggataat	660
gctgtggtgg	agtgtttctt	tggaacctta	aagtcggagt	gtttttatct	tgatgagttc	720
agtaataata	gcgaactgaa	ggatgctgtt	acggaatata	ttgaatacta	caacagcaga	780
agaattagcc	tgaattataa	aggtctgact	ccaattgaat	atcggaatca	gacctatatg	840
cctcgtgttt	aa					852

<210> 151

<211> 117

<212> DNA

<213> E. Coli

<400> 151

atgaaagttc	gtgcttccgt	caagaaatta	tgccgtaact	gcaaaatcgt	taagcgtgat	60
gggtgcatcc	gtgtgatttg	cagtgccgag	ccgaagcata	aacagcgcca	aggctga	117

<210> 152

<211> 1332

<212> DNA

<213> E. Coli

<400> 152

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cgcagactgc	tgtttgttat	cggtgcgctg	atttgtttcc	gtattggctc	ttttattccg	120
atccctggta	ttgatgccgc	tgtacttgcc	aaactgcttg	agcaacagcg	aggcaccatc	180
attgagatgt	ttaacatggt	ctctgggtgg	gctctcagcc	gtgcttctat	ctttgctctg	240
gggatcatgc	cgtatatattc	ggcgtcgatc	attatccagc	tgctgacggg	ggttcaccga	300
acgtttggcag	aaattaagaa	agaaggggag	tctggtcgct	gtaagatcag	ccagtacacc	360
cgctacggta	ctctgggtgct	ggcaatatcc	cagtcgatcg	gtattgctac	cggtctgccg	420
aatatgcctg	gtatgcaagg	cctgggtgatt	aaccggggct	ttgcattcta	cttcaccgct	480
gttgtaagtc	tggtcacagg	aaccatgttc	ctgatgtggt	tgggcgaaca	gattactgaa	540
cgaggtatcg	gcaacgggtat	ttcaatcatt	atcttcgccc	gtattgtcgc	gggactcccg	600
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caacgccgca	ttgtggtaaa	ctacgcgaaa	cgtcagcaag	gtcgtcgtgt	ctatgctgca	780
cagagcacac	atttaccgct	gaaagtgaat	atggcggggg	taatcccgcc	aatcttcgct	840
tccagtatta	ttctgttccc	ggcgaccatc	gcgtcatggg	tcggggggcg	tactggttgg	900
aactggctga	caacaatttc	gctgtatttg	cagcctgggc	aaccgcttta	tgtgttactc	960
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caaacggcga	agtatatcga	taaagtaatg	acccgcctga	ccctgggttg	tgcgctgtat	1140
attaccttta	tctgcctgat	cccgagggtc	atgcgtgatg	caatgaaagt	accgttctac	1200
ttcgggtgga	cctcactgct	tatcggtgtt	gtcgtgatta	tggactttat	ggctcaagtg	1260
caaactctga	tgatgtccag	tcagtatgag	tctgcattga	agaaggcgaa	cctgaaaggc	1320
tacggccgat	aa					1332

<210> 153

<211> 435

<212> DNA

<213> E. Coli

<400> 153

atgcgtttta	atactctgtc	tccggccgaa	ggctccaaaa	aggcgggtaa	acgcctgggt	60
cgtggtatcg	gttctggcct	cggtaaaaacc	ggtggctcgtg	gtcacaaagg	tcagaagtct	120
cggtttggcg	gtggcgtagc	tcgcggtttc	gaggggtggc	agatgcctct	gtaccgtcgt	180
ctgccgaaat	tcggcttcac	ttctcgtaaa	gcagcgatta	cagccgaaat	tcgtctgtct	240
gacctggcta	aagtagaagg	cggtgtagta	gacctgaaca	cgctgaaagc	ggctaacatt	300
atcggtatcc	agatcgagtt	cgcgaaagtg	atcctggctg	gcgaagtaac	gactccggta	360
actgttcgtg	gcctgcgtgt	tactaaaggc	gctcgtgctg	ctatcgaagc	tgctggcggt	420
aaaatcaggag	aataa					435

<210> 154

<211> 180
 <212> DNA
 <213> E. Coli

<400> 154
 atggcaaaaga ctattaaaat tactcaaacc cgcagtgcaa tcggctcgtct gccgaaacac 60
 aaggcaacgc tgcttgccct gggctctgct cgtattggtc acaccgtaga gcgcgaggat 120
 actcctgcta ttcgcggtat gatcaacgcg gtttccttca tggttaaaagt tgaggagtaa 180

<210> 155
 <211> 504
 <212> DNA
 <213> E. Coli

<400> 155
 atggctcaca tcgaaaaaca agctggcgaa ctgcaggaaa agctgatcgc ggtaaaccgc 60
 gtatctaaaa ccgttaaaagg tggctgtatt ttctccttca cagctctgac tgtagttggc 120
 gatggtaacg gtcgcgttg ttttggttac ggtaaagcgc gtgaagttcc agcagcgatc 180
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 ctgcaaacacc ctgttaaaagg tggtcacacg ggttctcgcg tattcatgca gccggcttcc 300
 gaaggtagcc gtatcatcgc cgggtggtgca atgcgcgcgcg ttctggaagt cgctggggtt 360
 cataacggtc tggctaaagc ctatggttcc accaaccgca tcaacgtggt tcgtgcaact 420
 attgatggcc tggaaaatat gaattctcca gaaatggtcg ctgccaaagc tggtaaatcc 480
 gttgaagaaa ttctggggaa ataa 504

<210> 156
 <211> 354
 <212> DNA
 <213> E. Coli

<400> 156
 atggataaga aatctgctcg tatccgtcgt gcgaccgcg cagcccgcaa gctccaggag 60
 ctgggcgcaa ctgcctcgtt ggtacatcgt accccgcgct acatttacgc acaggtaatt 120
 gcaccgaacg gttctgaagt tctggtagct gcttctactg tagaaaaagc tatcgtgaa 180
 caactgaagt acaccggtaa caaagacgcg gctgcagctg tgggtaaaagc tctcgtgaa 240
 cgcgctctgg aaaaaggcat caaagatgta tcctttgacc gttccgggtt ccaatatcat 300
 ggtcgtgtcc aggcactggc agatgctgcc cgtgaagctg gccttcagtt ctaa 354

<210> 157
 <211> 534
 <212> DNA
 <213> E. Coli

<400> 157
 atgtctcgtg ttgctaaagc accggtcgtt gttcctgccg gcgttgacgt aaaaatcaac 60
 ggtcagggtta ttacgatcaa aggtaaaaac ggcgagctga ctcgtactct caacgatgct 120
 gttgaagtta aacatgcaga taataccctg accttcggtc cgcgtgatgg ttacgcagac 180
 ggttgggcac aggtcgttac cgcgcgtgcc ctgctgaact caatggttat cgggtttacc 240
 gaaggccttca ctaagaagct gcagctggtt ggtgtaggtt accgtgcagc ggttaaaggc 300
 aatgtgatta acctgtctct gggtttctct catcctgttg accatcagct gcctgcgggt 360
 atcactgctg aatgtccgac tcagactgaa atcgtgctga aaggcgtgaa taagcagggtg 420
 atcggccagg ttgcagcgga tctgcgcgcc taccgtcgtc ctgagcctta taaaggcaag 480
 ggtgttcgtt acgccgacga agtcgtgctt accaaagagg ctaagaagaa gtaa 534

<210> 158
 <211> 393
 <212> DNA
 <213> E. Coli

<400> 158
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aacaaagctg	cggtcaccat	gccttcctcc	aagctgaaag	tggcaatcgc	caacgtgctg	120
aaggaagaag	gttttattga	agatttttaa	gttgaaggcg	acaccaagcc	tgaactggaa	180
cttactctga	agtattttcca	gggcaaagct	gtttagaaaa	gcattcagcg	tgtcagccgc	240
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atcgagttg	tttctacctc	taaagggtgt	atgactgatc	gtgcagcgcg	ccaggctggt	360
cttggtggcg	aaattatctg	ctacgtagcc	taa			393

<210> 159

<211> 306

<212> DNA

<213> E. Coli

<400> 159

atggctaagc	aatcaatgaa	agcacgcgaa	gtaaaacgcg	tagcttttagc	tgataaatac	60
ttcgcgaaac	gcgctgaact	gaaagcgatc	atctctgatg	tgaacgcttc	cgacgaagat	120
cgttggaacg	ctgtttctcaa	gctgcagact	ctgccgcgctg	attccagccc	gtctcgtcag	180
cgtaaccgct	gccgtcaaac	aggctcgtccg	catggttttcc	tcgaggaaagt	cggttgtagc	240
cgtattaagg	tccgtgaagc	cgctatgcgc	ggtgaaatcc	cggtctgtaa	aaaggctagc	300
tggtaa						306

<210> 160

<211> 540

<212> DNA

<213> E. Coli

<400> 160

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aactacaatt	ctgtcatgca	agtcctctcg	gtcgagaaga	tcacctgaa	catgggtgtt	120
ggtgaagcga	tcgctgacaa	aaaactgctg	gataacgcag	cagcagacct	ggcagcaatc	180
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tctttcgacg	gtcgtggtaa	ctacagcatg	ggtgtccgtg	agcagatcat	cttcccagaa	420
atcgactacg	ataaagtcga	ccgcgttcgt	ggtttggata	ttaccattac	cactactgcg	480
aaatctgacg	aagaaggccg	cgctctgctg	gctgcctttg	acttcccgtt	ccgcaagtaa	540

<210> 161

<211> 315

<212> DNA

<213> E. Coli

<400> 161

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aaacgcggta	aagttaagaa	tgctctgtct	tccggcaagg	tcattgttga	aggatatcaac	120
ctggttaaga	aacatcagaa	gccggttccg	gccctgaacc	aaccgggtgg	catcggtgaa	180
aaagaagccg	ctattcaggt	ttccaacgta	gcaatcttca	atgcccgaac	cggcaaggct	240
gaccgtgtag	gcttttagatt	cgaagacggt	aaaaaagtc	gtttcttcaa	gtctaacagc	300
gaaactatca	agtaa					315

<210> 162

<211> 372

<212> DNA

<213> E. Coli

<400> 162

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atcaccatca	aagaagcaat	tccgcgtggt	aagggtcaaaa	aagggtgatgt	gctgaaggcg	180
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ggtaatgctt	gtgttcttct	gaacaacaac	agcagacgac	ctatcggtac	gcgtattttt	300
gggccggtaa	ctcgtgagct	tcgtagttag	aagttcatga	aaattatctc	tctggcacca	360

gaagtactct aa

372

<210> 163
 <211> 567
 <212> DNA
 <213> E. Coli

<400> 163

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ccttgtgaaa	ttcatccaga	agatattgat	aaaaacatag	atcttggaca	agtcacgaca	180
acccatataa	accgggagca	tcatagcaat	aaagtggccg	tcgacattcg	cttgatcaac	240
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ttcgatagca	cggctaagac	aactgggtgt	acgcctttgt	tgagcaacac	cagtgcaggc	360
gaagcaactg	gggtcgggtg	acgactgatg	gacaaaaatg	acggtaacat	cgtattaggt	420
tcagccgcgc	cagatcttga	cctggatgca	agctcatcag	aacagacgct	gaacttttct	480
gcctggatgg	aacaaattga	taatgcagtc	gatgtcacgg	caggtgaagt	aaccgctaac	540
gcaacctacg	tgctggatta	taaataaa				567

<210> 164
 <211> 1284
 <212> DNA
 <213> E. Coli

<400> 164

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<210> 165
 <211> 1434
 <212> DNA
 <213> E. Coli

<400> 165

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<210> 166

<211> 2841

<212> DNA

<213> E. Coli

<400> 166

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<210> 167

<211> 1302

<212> DNA

<213> E. Coli

<400> 167

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<210> 168

<211> 213

<212> DNA

<213> E. Coli

<400> 168

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ggttacaaat	ctctggacga	aggtcagaaa	gtgtccttca	ccatcgaaag	cggcgctaaa	180
ggcccggcag	ctggtaacgt	aaccagcctg	taa			213

<210> 169

<211> 1572

<212> DNA

<213> E. Coli

<400> 169

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cgacatatgc	cagcaggcgg	cgtctgggtg	tttaacgctg	atcgccatga	agatgctatc	120
agtctggcga	atcaaacaat	tgcatcccag	gctgaaaccg	cacacgtcgc	ggtcattagc	180

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gatggctgcc	actggcgacg	aataccagaa	cccatgcgac	tgtagatga	tgctgtggag	1560
cgctcatcat	ga					1572

<210> 170

<211> 189

<212> DNA

<213> E. Coli

<400> 170

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ggctatctgg	cgcggcactc	tttgcgacgc	attcgcgaca	ccttacgttt	gttctttgct	120
aaacctcggt	atgttaaacc	ggccgggacg	ttacgccgca	cggaaaaagc	cagggcaacc	180
aaaaaatga						189

<210> 171

<211> 1680

<212> DNA

<213> E. Coli

<400> 171

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aacttccatc	cgctcctcaa	tttggtgttt	gccgcgtttc	tgctgatgcc	ccttccgcgc	180
tacagcctgc	atcgcttgcg	ccactggatt	gccctgccga	tcggctttgc	ttgtttctgg	240
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<210> 172

<211> 384

<212> DNA

<213> E. Coli

<400> 172

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<210> 173

<211> 306

<212> DNA

<213> E. Coli

<400> 173

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tggacgggcg	tgggcattgg	cgctgcaatc	gggtgtagtgc	tcggcgttct	gctgtcgcgt	300
cgtaa						306

<210> 174

<211> 405

<212> DNA

<213> E. Coli

<400> 174

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<210> 175

<211> 300

<212> DNA

<213> E. Coli

<400> 175

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cgctcgctgga	atatgctgct	aagtcgtcgc	tcctggcgcg	tggttggcag	tagcgtgatg	180
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gtatggagcg cctggcgtct ggtaaaccg accctcaagc agcaacagct tcgcggttaa 300

<210> 176
<211> 483
<212> DNA
<213> E. Coli

<400> 176
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gtagcgcgca ttttaatgcc gattctgttt attaccgctg gctggggaaa aattactggc 180
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gctgaaggcg tcaactcgct gatgttcattg aaaaacctga caatttctgg cggattcctg 420
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taa 483

<210> 177
<211> 891
<212> DNA
<213> E. Coli

<400> 177
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<210> 178
<211> 612
<212> DNA
<213> E. Coli

<400> 178
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<210> 179
<211> 177
<212> DNA

<213> E. Coli

<400> 179

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<210> 180

<211> 4281

<212> DNA

<213> E. Coli

<400> 180

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<210> 181

<211> 369

<212> DNA

<213> E. Coli

<400> 181

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ttagataaat	actctgttaa	aaatacggta	aaaactgaaa	caatggcgat	acaattagct	180
gaaatatatg	ttaggtatcg	ctatggcgaa	cggattgcag	aagaagaaaa	accatattta	240
attacggaac	taccagatag	ttgggttgtt	gagggagcaa	agttacctta	tgaagttgcg	300
ggtggtgtat	ttattataga	aattaataag	aaaaatggat	gtgttttgaa	tttctacat	360
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<210> 182

<211> 711

<212> DNA

<213> E. Coli

<400> 182

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cagcagtatg	ataaggagtc	ggggctgtac	tacaaccgga	accggtacta	cgatccgttg	180
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gggttgacat	gtccatcaac	aacagattgc	tcagatagat	gtagtgatta	tattaatcca	660
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<210> 183

<211> 261

<212> DNA

<213> E. Coli

<400> 183

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aaacattaca	taaaactatat	ggcaatacca	gaaaatgatg	gagtttttac	atggctccca	180
gatttttttc	cgcacgtagc	ggtggatata	tcaatatata	caaatgtaga	agatgattat	240
ttttttctta	tttttcccta	a				261

<210> 184

<211> 192

<212> DNA

<213> E. Coli

<400> 184

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ggtgaaatta	atgttacgca	ttatTTTTata	acaaatattg	gagctggatt	gcctgatgct	180
tgtgcagagt	aa					192

<210> 185

<211> 504

<212> DNA

<213> E. Coli

<400> 185

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gcggaaatgg	acgaacagtg	gggctatgtc	ggggctaaat	cgcgccagcg	ctggctgttt	180
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<210> 186

<211> 276

<212> DNA

<213> E. Coli

<400> 186

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ctgcagttca	cttacaccgc	ttctcaaccc	ggtacgcacc	agaaaatcat	tgatatggcc	180
atgaatggcg	ttggatgccg	ggcaacagcc	cgcattatgg	gcgttggcct	caacacgatt	240
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<210> 187

<211> 417

<212> DNA

<213> E. Coli

<400> 187

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agaaataatg	atgatttcac	aaaccctgat	ctacaagaac	ggttagtgat	cggggattat	360
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<210> 188
 <211> 1179
 <212> DNA
 <213> E. Coli

<400> 188

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<210> 189
 <211> 666
 <212> DNA
 <213> E. Coli

<400> 189

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atattaaagt	cgtggagtaa	agcaggaagt	tcatatgtca	ctgttgggag	ttgtaatgca	660
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<210> 190
 <211> 705
 <212> DNA
 <213> E. Coli

<400> 190

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gatgaagctc	acaatgtaat	gagcaatcta	tattaccctg	aagtaagaaa	aattgaagac	420
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tcgataattg	cattaatttc	cttcctaata	atcttttttt	gcaaacaaat	ggatattttt	540
catgttgaag	gttcttttgc	gtcttttattc	ttttttgtaa	ttttatcatt	ctcagtgaag	600
ggtattatct	ttgcttttgac	agttaagccc	agaactgaaa	gtcaagtcgg	aaaaatcccg	660
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<210> 191

<211> 285

<212> DNA

<213> E. Coli

<400> 191

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gagctggatc	acgacaaagt	catgaacatg	caagctaaag	ctgaattcta	cagcgaagtt	180
ctgaccatcg	ttgttgacgg	taaagaaatc	aaagttaaag	ctcaggacgt	acagcgtcac	240
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<210> 192

<211> 1977

<212> DNA

<213> E. Coli

<400> 192

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<210> 193

<211> 2634

<212> DNA

<213> E. Coli

<400> 193

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<210> 194

<211> 1572

<212> DNA

<213> E. Coli

<400> 194

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<210> 195

<211> 1140

<212> DNA

<213> E. Coli

<400> 195

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cgtaacgaca	ccgagcgctc	aattatgatt	aactccattg	caccacactg	ggacggtaac	180
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<210> 196

<211> 1371

<212> DNA

<213> E. Coli

<400> 196

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<210> 197

<211> 186

<212> DNA

<213> E. Coli

<400> 197

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tctgttcacc	gtgaagagat	ctaccagcgt	atccaggctg	aaaaatccca	gcagtccagt	180
tactaa						186

<210> 198

<211> 93

<212> DNA

<213> E. Coli

<400> 198

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gcatccgggg	ttcgaatccc	cgcctcaccg	cca			93

<210> 199

<211> 603

<212> DNA

<213> E. Coli

<400> 199

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<210> 200

<211> 597

<212> DNA

<213> E. Coli

<400> 200

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<210> 201

<211> 549

<212> DNA

<213> E. Coli

<400> 201

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aacgttggt	t	gcagatcct	ggacagaacg	ggtgctgcgc	tgacgttga	tggcgcgaca	420
tttagttcag	a	aaacaaccct	gaataacgga	accaatacca	ttcgtttcca	ggcgcgttat	480
tttgcaaccg	g	ggccgcaac	cccgggtgct	gctaattgcg	atgcgacctt	caaggttcag	540
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<210> 202

<211> 648

<212> DNA

<213> E. Coli

<400> 202

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agattatttc	t	tattagcgtc	gttgctgcca	atggttgctc	tggccggaaa	taaatggaat	180
accacgttgc	c	ggcgggaaa	tatgcaattt	cagggcgtca	ttattgcgga	aacttgccgg	240
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gatgatgaag	a	gaaacctcgt	accgattaat	cgctctccag	caaactggaa	acggctttat	540
tcaggctcta	c	ttcgctaca	tttcacgcgc	aaatatcgtg	ctaccggg	tcgggttact	600
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<210> 203

<211> 726

<212> DNA

<213> E. Coli

<400> 203

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gatcaggccg	c	cagaaaaatt	aagatttcgt	cgtagcgcga	attctctgac	gctgattaac	540
ccgacaccct	a	ttacctgac	ggtaacagag	ttgaatgccg	gaaccggggt	tcttgaaaat	600
gcattggtgc	c	tccaatggg	cgaaagcacg	gttaaattgc	cttctgatgc	aggaagcaat	660

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gaataa 726

<210> 204
<211> 2637
<212> DNA
<213> E. Coli

<400> 204
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cctttgtcat ctgccgacct ctattttaat ccgcgctttt tagcggatga tcccaggct 180
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<210> 205
<211> 531
<212> DNA
<213> E. Coli

<400> 205
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gccgctgaat	caaccaattt	tactgttgat	ctgatggaaa	acgcggcgaa	gcaattttaac	180
aacattggcg	cgacgactcc	tggtgttcca	tttcgtat	tgctgtcacc	ctgtggtaat	240
gccgtttctg	ccgtaaaggt	tggttttact	ggcggttcag	atagccacaa	tgccaacctg	300
cttgcaactg	aaaatacgg	gtcagcggct	tcgggactgg	gaatacagct	tctgaatgag	360
cagcaaaatc	aaataccct	taatgctcca	tcgtccgcgc	tttcgtggac	gaccctgacg	420
ccgggtaaac	caaatacgt	gaatttttac	gcccggttaa	tggcgacaca	ggtgcctgtc	480
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<210> 206

<211> 504

<212> DNA

<213> E. Coli

<400> 206

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gtttccacca	ccatgccac	ggttgatctc	ggcgatcttt	attctttcag	tcttatgtct	180
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actggcgcaa	ccaaaacagt	tcaggtggat	gattcctcac	aatcagcgca	cttcccgtta	420
caggtcagag	cattgacagt	aaatggcgga	gccactcagg	gaaccattca	ggcagtgatt	480
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<210> 207

<211> 903

<212> DNA

<213> E. Coli

<400> 207

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gtttatgtaa	accttgcgcc	cgctgtgaat	gtggggcaaa	acctggtcgt	ggatctttcg	180
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cgaggtcgcg	cttatggcgg	cggttatctc	aatttttccg	ggaccgtaaa	atatagtggc	300
agtagctatc	catttcctac	caccagcgaa	acgccgcgcg	ttgtttataa	ttcgagaacg	360
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<210> 208

<211> 1631

<212> DNA

<213> E. Coli

<400> 208

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tcggcgggta	atgctgggtt	ctgggcattg	cagttactcg	ataaagtaac	tccgtcacag	180
tggtgctgcaa	tcggtgtgct	gggtagcctg	gtttttggcc	tgctgacgta	tctgacaaat	240
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<210> 209

<211> 534

<212> DNA

<213> E. Coli

<400> 209

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gcataccgcg	atggttcttg	catatggacc	atctgtcggg	gtgccacagt	ggtggatgga	180
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tgggtggatta	aggatggcgg	acgcgattgc	cgcatctcgt	caaataactg	ttacggctcag	480
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<210> 210

<211> 312

<212> DNA

<213> E. Coli

<400> 210

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gccatggacc	gtggtgaagg	agctgcgctg	gagttttatg	aggcagcagc	cagaaggagc	180
gtccggcaag	tcttcctgga	agtagcagaa	aaattgtcag	aaaaagttga	gtcttatctg	240
cagcatcagt	actcctttaa	gattgaaaaat	cctgccaaata	agcacgagcg	tctcatcat	300
aaatatctat	ga					312

<210> 211

<211> 291

<212> DNA

<213> E. Coli

<400> 211

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tcggcgggta	atgctggttt	ctgggcattg	cagttactcg	ataaagtaac	tccgtcacag	180
tgggtgcaaa	tcggtgtgct	gggtagcctg	gtttttggcc	tgctgacgta	tctgacaaat	240

ctttattttca agatttaaaga agacaggcgt aaggctgcga gaggagagta a 291

<210> 212
 <211> 216
 <212> DNA
 <213> E. Coli

<400> 212
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 aattatcgaa ccttatttga aggtcaaaaag gttaccttct ctatagagag tgggtgctaaa 180
 ggtcctgcag cagcaaatgt catcattact gattaa 216

<210> 213
 <211> 1017
 <212> DNA
 <213> E. Coli

<400> 213
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 gtgaaagcca gatacaagggt gttgctgaaa aacgataacc aactggcgat gttattcacg 960
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<210> 214
 <211> 474
 <212> DNA
 <213> E. Coli

<400> 214
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 ttattgaaac aaatatgccg gcattatgca ggccctggact atattagtgg aggtgtatac 180
 ggctttggtc ataataataa tattgcgggtg gcgtatgtaa aggaaaaata tagaccgcga 240
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 acatatatta aatatgtcga aagtaagcgt tatgctttta gtacattatg cctgttccga 360
 gatgaagcga aatctttaca tgattattcc gtaagaaaat ttctgtgct ttctgatttt 420
 attgtgtcat ttatgttagg gattaaggaa ggtgcgaaca agtccctgat atga 474

<210> 215
 <211> 1119
 <212> DNA
 <213> E. Coli

<400> 215
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 gtccattctg ctaaagagtt aaaagaaagt tatccatggg ttaaatcatc tgagtttctc 180

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tcaaaagagc	tgaatgctac	gcattggatt	tgtctgcatg	atattacggc	caatgtcgtc	300
actaaaaaaa	gatatgtgta	ttgtcataac	cctgcacctt	tttataaagg	aattttattc	360
cgtgaaattc	ttatggagcc	tagctttttc	ttatttaaaa	tgctatacgg	gctgatatat	420
aaaataaaca	ttaaaaaaa	tactgcagtg	tttgttcaac	aattctggat	gaaagaaaaa	480
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<210> 216

<211> 591

<212> DNA

<213> E. Coli

<400> 216

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gatgcatttg	gacgtggcgt	gatttttttt	tccgataatg	tgcaagttaa	cgactatggt	240
catatcgcc	caattgagag	cgttacgata	ggtcgggata	cgcttattgc	aagtaaagta	300
tttattaccg	atcataatca	cggttccttt	aagcactctg	atccaatgag	ttcgccaaat	360
atacctccag	acatgcccac	gttggaaatc	tcagctggtg	taattggcca	gagggtttgg	420
ttgggtgaga	atgtgacggg	tttgccctgga	acaattattg	gtaatggagt	cgtagtcggc	480
gccaattctg	ttgtagagag	ttctattccc	gaaaatactg	tcattgctggg	agtaccagca	540
aaaatcataa	agaaatacaa	tcatgagacc	aaattatggg	aaaaagcata	g	591

<210> 217

<211> 993

<212> DNA

<213> E. Coli

<400> 217

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gataaagccg	cccttgccga	tttcatttga	gataatagaa	taggatatgc	agtgggatca	840
atcaaaagaa	tgcgaagagat	tggtgactcc	atgacaatag	aaacttataa	gcaaatttagt	900
gagaatacaa	aaattatttc	tcagaaaatt	cgaacaggaa	gttacttcag	ggatgttctt	960
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<210> 218

<211> 1167

<212> DNA

<213> E. Coli

<400> 218

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ttcgggacta	gcttacttag	ctatatgaat	ttgataagag	atgctgatgt	tgaagacaca	420
tcaagaaatt	tctcagcata	catgcagcca	atcattctaa	ctacttttgc	tttattttatt	480
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<210> 219

<211> 1104

<212> DNA

<213> E. Coli

<400> 219

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tacacagagg	actgtgaggg	tatccagatt	cataaatatg	gtgcacatat	ttttcatacc	180
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tctccactgg	cgattttataa	agacaaatta	ttcaaccttc	cttttaatat	gaatactttc	300
caccaaattg	ggggagttaa	agatcctcaa	gaagctcaaa	atatcattaa	tgctcagaaa	360
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gaggacttat	accaagcatt	gataaagggt	tatacggaga	agcagtgggg	aagaagtgca	480
aaagaattgc	ctgcatttat	tattaagcga	atcccagtga	gattttacgtt	tgataacaat	540
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gcgagtaaa	cccatagaat	catctacact	ggacccattg	atcagtactt	cgactatagg	720
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cttttttaaga	aatatagaga	gttagctagc	agagaagaca	aggttatatt	tggcgggcgt	1020
ttggccgagt	ataaatatta	tgatatgcat	caagtgatat	ctgccgctct	ttatcaagtg	1080
aaaaatataa	tgagtacgga	ttaa				1104

<210> 220

<211> 1116

<212> DNA

<213> E. Coli

<400> 220

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gaacctcctt	taactcctca	aaacgaacat	cagcgggtccg	ggctgcgctt	cgcccgtcgc	120
gtcagactac	cccgtgcggt	tgccctggct	ggcatgttct	taccgattgc	ttcaacgctg	180
gtttcacacc	cgccgcggg	ctggtggtgg	ctggtgttgg	tcggctgggc	gttcgtctgg	240
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aacttaaaaa	ccgatgcagt	attagcggga	atgtgggtag	gcgtaatggg	cgtaaacgtg	360
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cgtctgtttg	tcgcgggtct	ggtgttgatg	gtggtttcct	gccttgtcac	cctcgagctg	480
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<210> 221

<211> 1404

<212> DNA

<213> E. Coli

<400> 221

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agcagcgatt	acgttctgaa	cgctgatctg	gtgaacgacc	gtacctggga	tacttccaag	180
tctaactacg	gttacgggtat	tgttgctatg	aactctgatg	gtcacctgac	tatcaacggg	240
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gcctataccg	atgctaacta	cctcgggtgt	ggtgacgtag	atcaagactg	gtccgcgaac	1380
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<210> 222

<211> 669

<212> DNA

<213> E. Coli

<400> 222

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gagtttaata	atgaaaagca	agttatattt	tccagtgtat	tcaataacga	agatactttc	180
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ctggaattac	gcgacgtgca	gctcattggg	cataattcct	acgaacaaat	ccgcgcaaca	480
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atccatcaac	gtacacgcat	atcgcgttct	gtcgtcgcag	aagttctcgc	tgctttgcgt	600
aaaggcggct	atatcgaaat	gaataaaggc	aaactggtcg	ctatcaaccg	tttgccttca	660
gagtattaa						669

<210> 223
 <211> 255
 <212> DNA
 <213> E. Coli

<400> 223						
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attgttggtg	ctatcgaaacg	ttttgtgaaa	cacccgatct	acggtaaatt	catcaagcgt	120
acgaccaaac	tgcacgtaca	tgacgagaac	aacgaatgcg	gtatcgggtga	cgtgggttgaa	180
atccgcgaat	gccgtccgct	gtccaagact	aaatcctgga	cgctgggttcg	cggtgtagag	240
aaagcgggttc	tgtaa					255

<210> 224
 <211> 192
 <212> DNA
 <213> E. Coli

<400> 224						
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ctgctgcgtg	agcagttcaa	cctgcgtatg	caggctgcaa	gtggccagct	gcaacagtct	120
cacctgttga	agcaagtgcg	tcgcgatgtc	gcacgcgtta	agactttact	gaacgagaag	180
gcgggtgcgt	aa					192

<210> 225
 <211> 411
 <212> DNA
 <213> E. Coli

<400> 225						
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gcgagggtga	cggtatgttag	cttcggcagc	ttcggctctga	aagctgttgg	ccgtgggtcgt	120
ctgactgccc	gtcagatcga	agcagcacgt	cgtgctatga	cccgtgcagt	taagcgtcaa	180
ggtaagatct	ggatccgtgt	gttcccggac	aaaccgatca	ctgaaaagcc	gctggcagtg	240
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gtcctgtatg	aaatggacgg	tggtccggaa	gagctggccc	gtgaagcatt	caagctggca	360
gcagcgaaac	tgccgattaa	aaccaccttt	gtaactaaga	cggtgatgta	a	411

<210> 226
 <211> 702
 <212> DNA
 <213> E. Coli

<400> 226						
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cagtacctga	ctaagggaact	ggctaaagcg	tccgtatctc	gtatcgttat	cgagcgtccg	180
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gcaatgcgtc	tgggcgctaa	aggtattaaa	gttgaagtta	gcggccgtct	gggcggcgcg	480
gaaatcgcac	gtaccgaatg	gtaccgcgaa	ggtcgcgtac	cgctgcacac	tctgcgtgct	540
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tggatcttca	aaggcgagat	cctgggtggg	atggctgctg	ttgaacaacc	ggaaaaaccg	660
gctgctcagc	ctaaaaagca	gcagcgtaaa	ggccgtaaat	aa		702

<210> 227

<211> 333
 <212> DNA
 <213> E. Coli

<400> 227
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 aagaaagcgg ctgtactggt caagaaagt ctggaatctg ccattgctaa cgctgaacac 180
 aacgatggcg ctgacattga cgatctgaaa gttacgaaaa ttttcgtaga cgaaggcccg 240
 agcatgaagc gcattatgcc gcgtgcaaaa ggctgtgcag atcgcatcct gaagcgacc 300
 agccacatca ctgtggttgt gtccgatcgc tga 333

<210> 228
 <211> 279
 <212> DNA
 <213> E. Coli

<400> 228
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 aaagcgggtg aaagcggaga caagaagccc ctgcgcactt ggtcccgtcg ttcaacgac 120
 tttcctaaca tgatcgggtt gaccatcgct gtccataatg gtcgtcagca cgttccggt 180
 ttgttaaccg acgaaatggt tggtcacaaa ctgggtgaat tcgcaccgac tcgtacttat 240
 cgcgccacg ctgctgataa aaaagcgaag aagaaataa 279

<210> 229
 <211> 822
 <212> DNA
 <213> E. Coli

<400> 229
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 ggtggctgta acaacaatgg ccgtatcacc actcgctcata tcggtgggtg ccacaagcag 180
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<210> 230
 <211> 303
 <212> DNA
 <213> E. Coli

<400> 230
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 gcagaaatca aagctgctgt gcagaaactg tttgaagtcg aagtcgaagt cgtaaacacc 180
 ctggtagtta aagggaaagt taaacgtcac ggacagcgta tcggtcgtcg tagcgactgg 240
 aaaaaagctt acgtcaccc taaagaaggc cagaatctgg acttcgttgg cggcgctgag 300
 taa 303

<210> 231
 <211> 630
 <212> DNA

<213> E. Coli

<400> 231

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gctaaccgatg	gctaccgtgc	tattcaggtg	accaccgggtg	ctaaaaaagc	taaccgtgtg	180
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gaattccgcc	tggtggaag	cgaagagttc	actgtaggtc	agagcattag	cgttgaactg	300
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gacgtgagc	gcaacctgct	gctgggttaa	ggtgctgtcc	cgggtgcaac	cggtagcgac	600
ctgatcggtta	aaccagctgt	gaaggcgtaa				630

<210> 232

<211> 606

<212> DNA

<213> E. Coli

<400> 232

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<210> 233

<211> 312

<212> DNA

<213> E. Coli

<400> 233

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<210> 234

<211> 357

<212> DNA

<213> E. Coli

<400> 234

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<210> 235

<211> 198

<212> DNA

<213> E. Coli

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<210> 236

<211> 543

<212> DNA

<213> E. Coli

<400> 236

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<210> 237

<211> 1929

<212> DNA

<213> E. Coli

<400> 237

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<210> 238
 <211> 1353
 <212> DNA
 <213> E. Coli

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 <211> 2904
 <212> DNA
 <213> E. Coli

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<210> 240

<211> 120

<212> DNA

<213> E. Coli

<400> 240

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<210> 241

<211> 76

<212> DNA

<213> E. Coli

<400> 241

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<210> 242

<211> 1549

<212> DNA

<213> E. Coli

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<210> 243

<211> 221

<212> PRT

<213> E. Coli

<400> 243

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20     25     30
Leu Pro Val Ser Ile Leu Gly Phe His Thr Thr Trp Gly Ala Phe Ser
35     40     45
Phe Pro Phe Ile Phe Leu Ala Thr Asp Leu Thr Val Arg Ile Phe Gly
50     55     60
Ala Pro Leu Ala Arg Arg Ile Ile Phe Ala Val Met Ile Pro Ala Leu
65     70     75     80
Leu Ile Ser Tyr Val Ile Ser Ser Leu Phe Tyr Met Gly Ser Trp Gln
85     90     95
Gly Phe Gly Ala Leu Ala His Phe Asn Leu Phe Val Ala Arg Ile Ala
100    105    110
Thr Ala Ser Phe Met Ala Tyr Ala Leu Gly Gln Ile Leu Asp Val His
115    120    125
Val Phe Asn Arg Leu Arg Gln Ser Arg Arg Trp Trp Leu Ala Pro Thr
130    135    140
Ala Ser Thr Leu Phe Gly Asn Val Ser Asp Thr Leu Ala Phe Phe Phe
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Ile Ala Phe Trp Arg Ser Pro Asp Ala Phe Met Ala Glu His Trp Met
165    170    175
Glu Ile Ala Leu Val Asp Tyr Cys Phe Lys Val Leu Ile Ser Ile Val
180    185    190
Phe Phe Leu Pro Met Tyr Gly Val Leu Leu Asn Met Leu Leu Lys Arg
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Leu Ala Asp Lys Ser Glu Ile Asn Ala Leu Gln Ala Ser
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<210> 244

<211> 203

<212> PRT

<213> E. Coli

<400> 244

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Met Gly Leu Ala Ala Cys Asp Asp Lys Asp Thr Asn Ala Thr Ala Gln
          35           40           45
Gly Ser Val Ala Glu Ser Asn Ala Thr Gly Asn Pro Val Asn Leu Leu
          50           55           60
Asp Gly Lys Leu Ser Phe Ser Leu Pro Ala Asp Met Thr Asp Gln Ser
65           70           75           80
Gly Lys Leu Gly Thr Gln Ala Asn Asn Met His Val Trp Ser Asp Ala
          85           90           95
Thr Gly Gln Lys Ala Val Ile Val Ile Met Gly Asp Asp Pro Lys Glu
          100          105          110
Asp Leu Ala Val Leu Ala Lys Arg Leu Glu Asp Gln Gln Arg Ser Arg
          115          120          125
Asp Pro Gln Leu Gln Val Val Thr Asn Lys Ala Ile Glu Leu Lys Gly
130          135          140
His Lys Met Gln Gln Leu Asp Ser Ile Ile Ser Ala Lys Gly Gln Thr
145          150          155          160
Ala Tyr Ser Ser Val Ile Leu Gly Asn Val Gly Asn Gln Leu Leu Thr
          165          170          175
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          180          185          190
Ala Glu Asn Ile Ile Asn Thr Leu Val Ile Gln
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<210> 245

<211> 324

<212> PRT

<213> E. Coli

<400> 245

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          20           25           30
Glu Arg Gln Ala Ala Ala Gln Ala Ala Gly Asp Ser Leu Asp Lys
          35           40           45
Ala Thr Leu Lys Lys Val Ala Pro Lys Pro Gly Trp Leu Glu Thr Gly
          50           55           60
Ala Ser Val Phe Pro Val Leu Ala Ile Val Leu Ile Val Arg Ser Phe
65           70           75           80
Ile Tyr Glu Pro Phe Gln Ile Pro Ser Gly Ser Met Met Pro Thr Leu
          85           90           95
Leu Ile Gly Asp Phe Ile Leu Val Glu Lys Phe Ala Tyr Gly Ile Lys
          100          105          110
Asp Pro Ile Tyr Gln Lys Thr Leu Ile Glu Thr Gly His Pro Lys Arg
          115          120          125
Gly Asp Ile Val Val Phe Lys Tyr Pro Glu Asp Pro Lys Leu Asp Tyr
130          135          140
Ile Lys Arg Ala Val Gly Leu Pro Gly Asp Lys Val Thr Tyr Asp Pro
145          150          155          160
Val Ser Lys Glu Leu Thr Ile Gln Pro Gly Cys Ser Ser Gly Gln Ala
          165          170          175
Cys Glu Asn Ala Leu Pro Val Thr Tyr Ser Asn Val Glu Pro Ser Asp
          180          185          190
Phe Val Gln Thr Phe Ser Arg Arg Asn Gly Gly Glu Ala Thr Ser Gly

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195						200					205				
Phe	Phe	Glu	Val	Pro	Lys	Asn	Glu	Thr	Lys	Glu	Asn	Gly	Ile	Arg	Leu
210						215					220				
Ser	Glu	Arg	Lys	Glu	Thr	Leu	Gly	Asp	Val	Thr	His	Arg	Ile	Leu	Thr
225	230					235					240				
Val	Pro	Ile	Ala	Gln	Asp	Gln	Val	Gly	Met	Tyr	Tyr	Gln	Gln	Pro	Gly
245						250					255				
Gln	Gln	Leu	Ala	Thr	Trp	Ile	Val	Pro	Pro	Gly	Gln	Tyr	Phe	Met	Met
260						265					270				
Gly	Asp	Asn	Arg	Asp	Asn	Ser	Ala	Asp	Ser	Arg	Tyr	Trp	Gly	Phe	Val
275						280					285				
Pro	Glu	Ala	Asn	Leu	Val	Gly	Arg	Ala	Thr	Ala	Ile	Trp	Met	Ser	Phe
290						295					300				
Asp	Lys	Gln	Glu	Gly	Glu	Trp	Pro	Thr	Gly	Leu	Arg	Leu	Ser	Arg	Ile
305	310					315					320				
Gly	Gly	Ile	His												

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<210> 246
<211> 586
<212> PRT
<213> E. Coli
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				<400>	246											
Met	Thr	Ile	Thr	Lys	Leu	Ala	Trp	Arg	Asp	Leu	Val	Pro	Asp	Thr	Asp	
1				5					10					15		
Ser	Tyr	Gln	Glu	Ile	Phe	Ala	Gln	Pro	His	Leu	Ile	Asp	Glu	Asn	Asp	
			20					25					30			
Pro	Leu	Phe	Ser	Asp	Thr	Gln	Pro	Arg	Leu	Gln	Phe	Ala	Leu	Glu	Gln	
		35					40					45				
Leu	Leu	His	Thr	Arg	Ala	Ser	Ser	Ser	Phe	Met	Leu	Ala	Lys	Ala	Pro	
	50				55						60					
Glu	Glu	Ser	Glu	Tyr	Leu	Asn	Leu	Ile	Ala	Asn	Ala	Ala	Arg	Thr	Leu	
65				70						75					80	
Gln	Ser	Asp	Ala	Gly	Gln	Leu	Val	Gly	Gly	His	Tyr	Glu	Val	Ser	Gly	
				85					90					95		
His	Ser	Ile	Arg	Leu	Arg	His	Ala	Val	Ser	Ala	Asp	Asp	Asn	Phe	Ala	
			100					105					110			
Thr	Leu	Thr	Gln	Val	Val	Ala	Ala	Asp	Trp	Val	Glu	Ala	Glu	Gln	Leu	
		115					120					125				
Phe	Gly	Cys	Leu	Arg	Gln	Phe	Asn	Gly	Asp	Ile	Thr	Leu	Gln	Pro	Gly	
		130				135					140					
Leu	Val	His	Gln	Ala	Asn	Gly	Gly	Ile	Leu	Ile	Ile	Ser	Leu	Arg	Thr	
145				150						155					160	
Leu	Leu	Ala	Gln	Pro	Leu	Leu	Trp	Met	Arg	Leu	Lys	Asn	Ile	Val	Asn	
				165					170					175		
Arg	Glu	Arg	Phe	Asp	Trp	Val	Ala	Phe	Asp	Glu	Ser	Arg	Pro	Leu	Pro	
			180					185					190			
Val	Ser	Val	Pro	Ser	Met	Pro	Leu	Lys	Leu	Lys	Val	Ile	Leu	Val	Gly	
		195					200					205				
Glu	Arg	Glu	Ser	Leu	Ala	Asp	Phe	Gln	Glu	Met	Glu	Pro	Glu	Leu	Ser	
		210				215					220					
Glu	Gln	Ala	Ile	Tyr	Ser	Glu	Phe	Glu	Asp	Thr	Leu	Gln	Ile	Val	Asp	
225				230						235					240	
Ala	Glu	Ser	Val	Thr	Gln	Trp	Cys	Arg	Trp	Val	Thr	Phe	Thr	Ala	Arg	
				245					250					255		
His	Asn	His	Leu	Pro	Ala	Pro	Gly	Ala	Asp	Ala	Trp	Pro	Ile	Leu	Ile	
		260						265					270			
Arg	Glu	Ala	Ala	Arg	Tyr	Thr	Gly	Glu	Gln	Glu	Thr	Leu	Pro	Leu	Ser	


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      275              280              285
Pro Gln Trp Ile Leu Arg Gln Cys Lys Glu Val Ala Ser Leu Cys Asp
      290              295              300
Gly Asp Thr Phe Ser Gly Glu Gln Leu Asn Leu Met Leu Gln Gln Arg
305              310              315              320
Glu Trp Arg Glu Gly Phe Leu Ala Glu Arg Met Gln Asp Glu Ile Leu
      325              330              335
Gln Glu Gln Ile Leu Ile Glu Thr Glu Gly Glu Arg Ile Gly Gln Ile
      340              345              350
Asn Ala Leu Ser Val Ile Glu Phe Pro Gly His Pro Arg Ala Phe Gly
      355              360              365
Glu Pro Ser Arg Ile Ser Cys Val Val His Ile Gly Asp Gly Glu Phe
370              375              380
Thr Asp Ile Glu Arg Lys Ala Glu Leu Gly Gly Asn Ile His Ala Lys
385              390              395              400
Gly Met Met Ile Met Gln Ala Phe Leu Met Ser Glu Leu Gln Leu Glu
      405              410              415
Gln Gln Ile Pro Phe Ser Ala Ser Leu Thr Phe Glu Gln Ser Tyr Ser
      420              425              430
Glu Val Asp Gly Asp Ser Ala Ser Met Ala Glu Leu Cys Ala Leu Ile
      435              440              445
Ser Ala Leu Ala Asp Val Pro Val Asn Gln Ser Ile Ala Ile Thr Gly
450              455              460
Ser Val Asp Gln Phe Gly Arg Ala Gln Pro Val Gly Gly Leu Asn Glu
465              470              475              480
Lys Ile Glu Gly Phe Phe Ala Ile Cys Gln Gln Arg Glu Leu Thr Gly
      485              490              495
Lys Gln Gly Val Ile Ile Pro Thr Ala Asn Val Arg His Leu Ser Leu
      500              505              510
His Ser Glu Leu Val Lys Ala Val Glu Glu Gly Lys Phe Thr Ile Trp
      515              520              525
Ala Val Asp Asp Val Thr Asp Ala Leu Pro Leu Leu Leu Asn Leu Val
530              535              540
Trp Asp Gly Glu Gly Gln Thr Thr Leu Met Gln Thr Ile Gln Glu Arg
545              550              555              560
Ile Ala Gln Ala Ser Gln Gln Glu Gly Arg His Arg Phe Pro Trp Pro
      565              570              575
Leu Arg Trp Leu Asn Trp Phe Ile Pro Asn
      580              585

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<210> 247
 <211> 394
 <212> PRT
 <213> E. Coli

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      <400> 247
Met Ser Lys Glu Lys Phe Glu Arg Thr Lys Pro His Val Asn Val Gly
 1              5              10              15
Thr Ile Gly His Val Asp His Gly Lys Thr Thr Leu Thr Ala Ala Ile
      20              25              30
Thr Thr Val Leu Ala Lys Thr Tyr Gly Gly Ala Ala Arg Ala Phe Asp
      35              40              45
Gln Ile Asp Asn Ala Pro Glu Lys Ala Arg Gly Ile Thr Ile Asn
      50              55              60
Thr Ser His Val Glu Tyr Asp Thr Pro Thr Arg His Tyr Ala His Val
65              70              75              80
Asp Cys Pro Gly His Ala Asp Tyr Val Lys Asn Met Ile Thr Gly Ala
      85              90              95
Ala Gln Met Asp Gly Ala Ile Leu Val Val Ala Ala Thr Asp Gly Pro
      100              105              110

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Met Pro Gln Thr Arg Glu His Ile Leu Leu Gly Arg Gln Val Gly Val
 115 120 125
 Pro Tyr Ile Ile Val Phe Leu Asn Lys Cys Asp Met Val Asp Asp Glu
 130 135 140
 Glu Leu Leu Glu Leu Val Glu Met Glu Val Arg Glu Leu Leu Ser Gln
 145 150 155 160
 Tyr Asp Phe Pro Gly Asp Asp Thr Pro Ile Val Arg Gly Ser Ala Leu
 165 170 175
 Lys Ala Leu Glu Gly Asp Ala Glu Trp Glu Ala Lys Ile Leu Glu Leu
 180 185 190
 Ala Gly Phe Leu Asp Ser Tyr Ile Pro Glu Pro Glu Arg Ala Ile Asp
 195 200 205
 Lys Pro Phe Leu Leu Pro Ile Glu Asp Val Phe Ser Ile Ser Gly Arg
 210 215 220
 Gly Thr Val Val Thr Gly Arg Val Glu Arg Gly Ile Ile Lys Val Gly
 225 230 235 240
 Glu Glu Val Glu Ile Val Gly Ile Lys Glu Thr Gln Lys Ser Thr Cys
 245 250 255
 Thr Gly Val Glu Met Phe Arg Lys Leu Leu Asp Glu Gly Arg Ala Gly
 260 265 270
 Glu Asn Val Gly Val Leu Leu Arg Gly Ile Lys Arg Glu Glu Ile Glu
 275 280 285
 Arg Gly Gln Val Leu Ala Lys Pro Gly Thr Ile Lys Pro His Thr Lys
 290 295 300
 Phe Glu Ser Glu Val Tyr Ile Leu Ser Lys Asp Glu Gly Gly Arg His
 305 310 315 320
 Thr Pro Phe Phe Lys Gly Tyr Arg Pro Gln Phe Tyr Phe Arg Thr Thr
 325 330 335
 Asp Val Thr Gly Thr Ile Glu Leu Pro Glu Gly Val Glu Met Val Met
 340 345 350
 Pro Gly Asp Asn Ile Lys Met Val Val Thr Leu Ile His Pro Ile Ala
 355 360 365
 Met Asp Asp Gly Leu Arg Phe Ala Ile Arg Glu Gly Gly Arg Thr Val
 370 375 380
 Gly Ala Gly Val Val Ala Lys Val Leu Gly
 385 390

<210> 248

<211> 704

<212> PRT

<213> E. Coli

<400> 248

Met Ala Arg Thr Thr Pro Ile Ala Arg Tyr Arg Asn Ile Gly Ile Ser
 1 5 10 15
 Ala His Ile Asp Ala Gly Lys Thr Thr Thr Glu Arg Ile Leu Phe
 20 25 30
 Tyr Thr Gly Val Asn His Lys Ile Gly Glu Val His Asp Gly Ala Ala
 35 40 45
 Thr Met Asp Trp Met Glu Gln Glu Gln Glu Arg Gly Ile Thr Ile Thr
 50 55 60
 Ser Ala Ala Thr Thr Ala Phe Trp Ser Gly Met Ala Lys Gln Tyr Glu
 65 70 75 80
 Pro His Arg Ile Asn Ile Ile Asp Thr Pro Gly His Val Asp Phe Thr
 85 90 95
 Ile Glu Val Glu Arg Ser Met Arg Val Leu Asp Gly Ala Val Met Val
 100 105 110
 Tyr Cys Ala Val Gly Gly Val Gln Pro Gln Ser Glu Thr Val Trp Arg
 115 120 125

Gln	Ala	Asn	Lys	Tyr	Lys	Val	Pro	Arg	Ile	Ala	Phe	Val	Asn	Lys	Met
130						135					140				
Asp	Arg	Met	Gly	Ala	Asn	Phe	Leu	Lys	Val	Val	Asn	Gln	Ile	Lys	Thr
145					150					155					160
Arg	Leu	Gly	Ala	Asn	Pro	Val	Pro	Leu	Gln	Leu	Ala	Ile	Gly	Ala	Glu
				165					170					175	
Glu	His	Phe	Thr	Gly	Val	Val	Asp	Leu	Val	Lys	Met	Lys	Ala	Ile	Asn
			180					185					190		
Trp	Asn	Asp	Ala	Asp	Gln	Gly	Val	Thr	Phe	Glu	Tyr	Glu	Asp	Ile	Pro
	195						200					205			
Ala	Asp	Met	Val	Glu	Leu	Ala	Asn	Glu	Trp	His	Gln	Asn	Leu	Ile	Glu
	210					215					220				
Ser	Ala	Ala	Glu	Ala	Ser	Glu	Glu	Leu	Met	Glu	Lys	Tyr	Leu	Gly	Gly
225					230					235					240
Glu	Glu	Leu	Thr	Glu	Ala	Glu	Ile	Lys	Gly	Ala	Leu	Arg	Gln	Arg	Val
				245					250					255	
Leu	Asn	Asn	Glu	Ile	Ile	Leu	Val	Thr	Cys	Gly	Ser	Ala	Phe	Lys	Asn
			260					265					270		
Lys	Gly	Val	Gln	Ala	Met	Leu	Asp	Ala	Val	Ile	Asp	Tyr	Leu	Pro	Ser
	275						280					285			
Pro	Val	Asp	Val	Pro	Ala	Ile	Asn	Gly	Ile	Leu	Asp	Asp	Gly	Lys	Asp
	290					295					300				
Thr	Pro	Ala	Glu	Arg	His	Ala	Ser	Asp	Asp	Glu	Pro	Phe	Ser	Ala	Leu
305					310					315					320
Ala	Phe	Lys	Ile	Ala	Thr	Asp	Pro	Phe	Val	Gly	Asn	Leu	Thr	Phe	Phe
				325					330					335	
Arg	Val	Tyr	Ser	Gly	Val	Val	Asn	Ser	Gly	Asp	Thr	Val	Leu	Asn	Ser
			340					345					350		
Val	Lys	Ala	Ala	Arg	Glu	Arg	Phe	Gly	Arg	Ile	Val	Gln	Met	His	Ala
	355						360					365			
Asn	Lys	Arg	Glu	Glu	Ile	Lys	Glu	Val	Arg	Ala	Gly	Asp	Ile	Ala	Ala
	370					375					380				
Ala	Ile	Gly	Leu	Lys	Asp	Val	Thr	Thr	Gly	Asp	Thr	Leu	Cys	Asp	Pro
385					390					395					400
Asp	Ala	Pro	Ile	Ile	Leu	Glu	Arg	Met	Glu	Phe	Pro	Glu	Pro	Val	Ile
				405					410					415	
Ser	Ile	Ala	Val	Glu	Pro	Lys	Thr	Lys	Ala	Asp	Gln	Glu	Lys	Met	Gly
			420					425					430		
Leu	Ala	Leu	Gly	Arg	Leu	Ala	Lys	Glu	Asp	Pro	Ser	Phe	Arg	Val	Trp
	435						440					445			
Thr	Asp	Glu	Glu	Ser	Asn	Gln	Thr	Ile	Ile	Ala	Gly	Met	Gly	Glu	Leu
	450					455					460				
His	Leu	Asp	Ile	Ile	Val	Asp	Arg	Met	Lys	Arg	Glu	Phe	Asn	Val	Glu
465					470					475					480
Ala	Asn	Val	Gly	Lys	Pro	Gln	Val	Ala	Tyr	Arg	Glu	Thr	Ile	Arg	Gln
				485					490					495	
Lys	Val	Thr	Asp	Val	Glu	Gly	Lys	His	Ala	Lys	Gln	Ser	Gly	Gly	Arg
			500					505					510		
Gly	Gln	Tyr	Gly	His	Val	Val	Ile	Asp	Met	Tyr	Pro	Leu	Glu	Pro	Gly
	515						520					525			
Ser	Asn	Pro	Lys	Gly	Tyr	Glu	Phe	Ile	Asn	Asp	Ile	Lys	Gly	Gly	Val
	530					535					540				
Ile	Pro	Gly	Glu	Tyr	Ile	Pro	Ala	Val	Asp	Lys	Gly	Ile	Gln	Glu	Gln
545					550					555					560
Leu	Lys	Ala	Gly	Pro	Leu	Ala	Gly	Tyr	Pro	Val	Val	Asp	Met	Gly	Ile
				565					570					575	
Arg	Leu	His	Phe	Gly	Ser	Tyr	His	Asp	Val	Asp	Ser	Ser	Glu	Leu	Ala
			580					585					590		
Phe	Lys	Leu	Ala	Ala	Ser	Ile	Ala	Phe	Lys	Glu	Gly	Phe	Lys	Lys	Ala
	595						600					605			
Lys	Pro	Val	Leu	Leu	Glu	Pro	Ile	Met	Lys	Val	Glu	Val	Glu	Thr	Pro

610	615	620
Glu Glu Asn Thr Gly Asp Val Ile Gly Asp Leu Ser Arg Arg Arg Gly		
625	630	635
Met Leu Lys Gly Gln Glu Ser Glu Val Thr Gly Val Lys Ile His Ala		
	645	650
Glu Val Pro Leu Ser Glu Met Phe Gly Tyr Ala Thr Gln Leu Arg Ser		
	660	665
Leu Thr Lys Gly Arg Ala Ser Tyr Thr Met Glu Phe Leu Lys Tyr Asp		
	675	680
Glu Ala Pro Ser Asn Val Ala Gln Ala Val Ile Glu Ala Arg Gly Lys		
690	695	700

<210> 249
 <211> 179
 <212> PRT
 <213> E. Coli

<400> 249

Met	Pro	Arg	Arg	Arg	Val	Ile	Gly	Gln	Arg	Lys	Ile	Leu	Pro	Asp	Pro
1				5					10					15	
Lys	Phe	Gly	Ser	Glu	Leu	Leu	Ala	Lys	Phe	Val	Asn	Ile	Leu	Met	Val
			20					25					30		
Asp	Gly	Lys	Lys	Ser	Thr	Ala	Glu	Ser	Ile	Val	Tyr	Ser	Ala	Leu	Glu
		35					40					45			
Thr	Leu	Ala	Gln	Arg	Ser	Gly	Lys	Ser	Glu	Leu	Glu	Ala	Phe	Glu	Val
		50				55					60				
Ala	Leu	Glu	Asn	Val	Arg	Pro	Thr	Val	Glu	Val	Lys	Ser	Arg	Arg	Val
65					70					75					80
Gly	Gly	Ser	Thr	Tyr	Gln	Val	Pro	Val	Glu	Val	Arg	Pro	Val	Arg	Arg
			85					90						95	
Asn	Ala	Leu	Ala	Met	Arg	Trp	Ile	Val	Glu	Ala	Ala	Arg	Lys	Arg	Gly
			100					105					110		
Asp	Lys	Ser	Met	Ala	Leu	Arg	Leu	Ala	Asn	Glu	Leu	Ser	Asp	Ala	Ala
		115					120					125			
Glu	Asn	Lys	Gly	Thr	Ala	Val	Lys	Lys	Arg	Glu	Asp	Val	His	Arg	Met
	130					135					140				
Ala	Glu	Ala	Asn	Lys	Ala	Phe	Ala	His	Tyr	Arg	Trp	Leu	Ser	Leu	Arg
145					150					155					160
Ser	Phe	Ser	His	Gln	Ala	Gly	Ala	Ser	Ser	Lys	Gln	Pro	Ala	Leu	Gly
				165					170					175	

Tyr Leu Asn

<210> 250
 <211> 124
 <212> PRT
 <213> E. Coli

<400> 250

Met	Ala	Thr	Val	Asn	Gln	Leu	Val	Arg	Lys	Pro	Arg	Ala	Arg	Lys	Val
1				5					10					15	
Ala	Lys	Ser	Asn	Val	Pro	Ala	Leu	Glu	Ala	Cys	Pro	Gln	Lys	Arg	Gly
			20					25					30		
Val	Cys	Thr	Arg	Val	Tyr	Thr	Thr	Thr	Pro	Lys	Lys	Pro	Asn	Ser	Ala
		35					40					45			
Leu	Arg	Lys	Val	Cys	Arg	Val	Arg	Leu	Thr	Asn	Gly	Phe	Glu	Val	Thr
	50					55					60				
Ser	Tyr	Ile	Gly	Gly	Glu	Gly	His	Asn	Leu	Gln	Glu	His	Ser	Val	Ile
65					70					75					80

Leu Ile Arg Gly Gly Arg Val Lys Asp Leu Pro Gly Val Arg Tyr His
 85 90 95
 Thr Val Arg Gly Ala Leu Asp Cys Ser Gly Val Lys Asp Arg Lys Gln
 100 105 110
 Ala Arg Ser Lys Tyr Gly Val Lys Arg Pro Lys Ala
 115 120

<210> 251
 <211> 165
 <212> PRT
 <213> E. Coli

<400> 251
 Met Ala Leu Asn Leu Gln Asp Lys Gln Ala Ile Val Ala Glu Val Ser
 1 5 10 15
 Glu Val Ala Lys Gly Ala Leu Ser Ala Val Val Ala Asp Ser Arg Gly
 20 25 30
 Val Thr Val Asp Lys Met Thr Glu Leu Arg Lys Ala Gly Arg Glu Ala
 35 40 45
 Gly Val Tyr Met Arg Val Val Arg Asn Thr Leu Leu Arg Arg Ala Val
 50 55 60
 Glu Gly Thr Pro Phe Glu Cys Leu Lys Asp Ala Phe Val Gly Pro Thr
 65 70 75 80
 Leu Ile Ala Tyr Ser Met Glu His Pro Gly Ala Ala Ala Arg Leu Phe
 85 90 95
 Lys Glu Phe Ala Lys Ala Asn Ala Lys Phe Glu Val Lys Ala Ala Ala
 100 105 110
 Phe Glu Gly Glu Leu Ile Pro Ala Ser Gln Ile Asp Arg Leu Ala Thr
 115 120 125
 Leu Pro Thr Tyr Glu Glu Ala Ile Ala Arg Leu Met Ala Thr Met Lys
 130 135 140
 Glu Ala Ser Ala Gly Lys Leu Val Arg Thr Leu Ala Ala Val Arg Asp
 145 150 155 160
 Ala Lys Glu Ala Ala
 165

<210> 252
 <211> 121
 <212> PRT
 <213> E. Coli

<400> 252
 Met Ser Ile Thr Lys Asp Gln Ile Ile Glu Ala Val Ala Ala Met Ser
 1 5 10 15
 Val Met Asp Val Val Glu Leu Ile Ser Ala Met Glu Glu Lys Phe Gly
 20 25 30
 Val Ser Ala Ala Ala Val Ala Val Ala Ala Gly Pro Val Glu Ala
 35 40 45
 Ala Glu Glu Lys Thr Glu Phe Asp Val Ile Leu Lys Ala Ala Gly Ala
 50 55 60
 Asn Lys Val Ala Val Ile Lys Ala Val Arg Gly Ala Thr Gly Leu Gly
 65 70 75 80
 Leu Lys Glu Ala Lys Asp Leu Val Glu Ser Ala Pro Ala Ala Leu Lys
 85 90 95
 Glu Gly Val Ser Lys Asp Asp Ala Glu Ala Leu Lys Lys Ala Leu Glu
 100 105 110
 Glu Ala Gly Ala Glu Val Glu Val Lys
 115 120

<210> 253
 <211> 714
 <212> PRT
 <213> E. Coli

<400> 253
 Met Ser Arg Ile Ile Met Leu Ile Pro Thr Gly Thr Ser Val Gly Leu
 1 5 10 15
 Thr Ser Val Ser Leu Gly Val Ile Arg Ala Met Glu Arg Lys Gly Val
 20 25 30
 Arg Leu Ser Val Phe Lys Pro Ile Ala Gln Pro Arg Thr Gly Gly Asp
 35 40 45
 Ala Pro Asp Gln Thr Thr Thr Ile Val Arg Ala Asn Ser Ser Thr Thr
 50 55 60
 Thr Ala Ala Glu Pro Leu Lys Met Ser Tyr Val Glu Gly Leu Leu Ser
 65 70 75 80
 Ser Asn Gln Lys Asp Val Leu Met Glu Glu Ile Val Ala Asn Tyr His
 85 90 95
 Ala Asn Thr Lys Asp Ala Glu Val Val Leu Val Glu Gly Leu Val Pro
 100 105 110
 Thr Arg Lys His Gln Phe Ala Gln Ser Leu Asn Tyr Glu Ile Ala Lys
 115 120 125
 Thr Leu Asn Ala Glu Ile Val Phe Val Met Ser Gln Gly Thr Asp Thr
 130 135 140
 Pro Glu Gln Leu Lys Glu Arg Ile Glu Leu Thr Arg Asn Ser Phe Gly
 145 150 155 160
 Gly Ala Lys Asn Thr Asn Ile Thr Gly Val Ile Val Asn Lys Leu Asn
 165 170 175
 Ala Pro Val Asp Glu Gln Gly Arg Thr Arg Pro Asp Leu Ser Glu Ile
 180 185 190
 Phe Asp Asp Ser Ser Lys Ala Lys Val Asn Asn Val Asp Pro Ala Lys
 195 200 205
 Leu Gln Glu Ser Ser Pro Leu Pro Val Leu Gly Ala Val Pro Trp Ser
 210 215 220
 Phe Asp Leu Ile Ala Thr Arg Ala Ile Asp Met Ala Arg His Leu Asn
 225 230 235 240
 Ala Thr Ile Ile Asn Glu Gly Asp Ile Asn Thr Arg Arg Val Lys Ser
 245 250 255
 Val Thr Phe Cys Ala Arg Ser Ile Pro His Met Leu Glu His Phe Arg
 260 265 270
 Ala Gly Ser Leu Leu Val Thr Ser Ala Asp Arg Pro Asp Val Leu Val
 275 280 285
 Ala Ala Cys Leu Ala Ala Met Asn Gly Val Glu Ile Gly Ala Leu Leu
 290 295 300
 Leu Thr Gly Gly Tyr Glu Met Asp Ala Arg Ile Ser Lys Leu Cys Glu
 305 310 315 320
 Arg Ala Phe Ala Thr Gly Leu Pro Val Phe Met Val Asn Thr Asn Thr
 325 330 335
 Trp Gln Thr Ser Leu Ser Leu Gln Ser Phe Asn Leu Glu Val Pro Val
 340 345 350
 Asp Asp His Glu Arg Ile Glu Lys Val Gln Glu Tyr Val Ala Asn Tyr
 355 360 365
 Ile Asn Ala Asp Trp Ile Glu Ser Leu Thr Ala Thr Ser Glu Arg Ser
 370 375 380
 Arg Arg Leu Ser Pro Pro Ala Phe Arg Tyr Gln Leu Thr Glu Leu Ala
 385 390 395 400
 Arg Lys Ala Gly Lys Arg Ile Val Leu Pro Glu Gly Asp Glu Pro Arg
 405 410 415
 Thr Val Lys Ala Ala Ala Ile Cys Ala Glu Arg Gly Ile Ala Thr Cys
 420 425 430

Val Leu Leu Gly Asn Pro Ala Glu Ile Asn Arg Val Ala Ala Ser Gln
 435 440 445
 Gly Val Glu Leu Gly Ala Gly Ile Glu Ile Val Asp Pro Glu Val Val
 450 455 460
 Arg Glu Ser Tyr Val Gly Arg Leu Val Glu Leu Arg Lys Asn Lys Gly
 465 470 475 480
 Met Thr Glu Thr Val Ala Arg Glu Gln Leu Glu Asp Asn Val Val Leu
 485 490 495
 Gly Thr Leu Met Leu Glu Gln Asp Glu Val Asp Gly Leu Val Ser Gly
 500 505 510
 Ala Val His Thr Thr Ala Asn Thr Ile Arg Pro Pro Leu Gln Leu Ile
 515 520 525
 Lys Thr Ala Pro Gly Ser Ser Leu Val Ser Ser Val Phe Phe Met Leu
 530 535 540
 Leu Pro Glu Gln Val Tyr Val Tyr Gly Asp Cys Ala Ile Asn Pro Asp
 545 550 555 560
 Pro Thr Ala Glu Gln Leu Ala Glu Ile Ala Ile Gln Ser Ala Asp Ser
 565 570 575
 Ala Ala Ala Phe Gly Ile Glu Pro Arg Val Ala Met Leu Ser Tyr Ser
 580 585 590
 Thr Gly Thr Ser Gly Ala Gly Ser Asp Val Glu Lys Val Arg Glu Ala
 595 600 605
 Thr Arg Leu Ala Gln Glu Lys Arg Pro Asp Leu Met Ile Asp Gly Pro
 610 615 620
 Leu Gln Tyr Asp Ala Ala Val Met Ala Asp Val Ala Lys Ser Lys Ala
 625 630 635 640
 Pro Asn Ser Pro Val Ala Gly Arg Ala Thr Val Phe Ile Phe Pro Asp
 645 650 655
 Leu Asn Thr Gly Asn Thr Thr Tyr Lys Ala Val Gln Arg Ser Ala Asp
 660 665 670
 Leu Ile Ser Ile Gly Pro Met Leu Gln Gly Met Arg Lys Pro Val Asn
 675 680 685
 Asp Leu Ser Arg Gly Ala Leu Val Asp Asp Ile Val Tyr Thr Ile Ala
 690 695 700
 Leu Thr Ala Ile Gln Ser Ala Gln Gln Gln
 705 710

<210> 254

<211> 588

<212> PRT

<213> E. Coli

<400> 254

Met Asn Asn Ser Ile Asn His Lys Phe His His Ile Ser Arg Ala Glu
 1 5 10 15
 Tyr Gln Glu Leu Ala Val Ser Arg Gly Asp Ala Val Ala Asp Tyr
 20 25 30
 Ile Ile Asp Asn Val Ser Ile Leu Asp Leu Ile Asn Gly Gly Glu Ile
 35 40 45
 Ser Gly Pro Ile Val Ile Lys Gly Arg Tyr Ile Ala Gly Val Gly Ala
 50 55 60
 Glu Tyr Thr Asp Ala Pro Ala Leu Gln Arg Ile Asp Ala Arg Gly Ala
 65 70 75 80
 Thr Ala Val Pro Gly Phe Ile Asp Ala His Leu His Ile Glu Ser Ser
 85 90 95
 Met Met Thr Pro Val Thr Phe Glu Thr Ala Thr Leu Pro Arg Gly Leu
 100 105 110
 Thr Thr Val Ile Cys Asp Pro His Glu Ile Val Asn Val Met Gly Glu
 115 120 125
 Ala Gly Phe Ala Trp Phe Ala Arg Cys Ala Glu Gln Ala Arg Gln Asn

130	135	140
Gln Tyr Leu Gln Val Ser Ser Cys Val Pro Ala Leu Glu Gly Cys Asp		
145	150	155
Val Asn Gly Ala Ser Phe Thr Leu Glu Gln Met Leu Ala Trp Arg Asp		160
	165	170
His Pro Gln Val Thr Gly Leu Ala Glu Met Met Asp Tyr Pro Gly Val		175
	180	185
Ile Ser Gly Gln Asn Ala Leu Leu Asp Lys Leu Asp Ala Phe Arg His		190
	195	200
Leu Thr Leu Asp Gly His Cys Pro Gly Leu Gly Gly Lys Glu Leu Asn		205
	210	215
Ala Tyr Ile Thr Ala Gly Ile Glu Asn Cys His Glu Ser Tyr Gln Leu		220
225	230	235
Glu Glu Gly Arg Arg Lys Leu Gln Leu Gly Met Ser Leu Met Ile Arg		240
	245	250
Glu Gly Ser Ala Ala Arg Asn Leu Asn Ala Leu Ala Pro Leu Ile Asn		255
	260	265
Glu Phe Asn Ser Pro Gln Cys Met Leu Cys Thr Asp Asp Arg Asn Pro		270
	275	280
Trp Glu Ile Ala His Glu Gly His Ile Asp Ala Leu Ile Arg Arg Leu		285
290	295	300
Ile Glu Gln His Asn Val Pro Leu His Val Ala Tyr Arg Val Ala Ser		305
	310	315
Trp Ser Thr Ala Arg His Phe Gly Leu Asn His Leu Gly Leu Leu Ala		320
	325	330
Pro Gly Lys Gln Ala Asp Ile Val Leu Leu Ser Asp Ala Arg Lys Val		335
	340	345
Thr Val Gln Gln Val Leu Val Lys Gly Glu Pro Ile Asp Ala Gln Thr		350
	355	360
Leu Gln Ala Glu Glu Ser Ala Arg Leu Ala Gln Ser Ala Pro Pro Tyr		365
370	375	380
Gly Asn Thr Ile Ala Arg Gln Pro Val Ser Ala Ser Asp Phe Ala Leu		385
385	390	395
Gln Phe Thr Pro Gly Lys Arg Tyr Arg Val Ile Asp Val Ile His Asn		400
	405	410
Glu Leu Ile Thr His Ser His Ser Ser Val Tyr Ser Glu Asn Gly Phe		415
	420	425
Asp Arg Asp Asp Val Ser Phe Ile Ala Val Leu Glu Arg Tyr Gly Gln		430
	435	440
Arg Leu Ala Pro Ala Cys Gly Leu Leu Gly Gly Phe Gly Leu Asn Glu		445
450	455	460
Gly Ala Leu Ala Ala Thr Val Ser His Asp Ser His Asn Ile Val Val		465
465	470	475
Ile Gly Arg Ser Ala Glu Glu Met Ala Leu Ala Val Asn Gln Val Ile		480
	485	490
Gln Asp Gly Gly Gly Leu Cys Val Val Arg Asn Gly Gln Val Gln Ser		495
	500	505
His Leu Pro Leu Pro Ile Ala Gly Leu Met Ser Thr Asp Thr Ala Gln		510
	515	520
Ser Leu Ala Glu Gln Ile Asp Ala Leu Lys Ala Ala Arg Glu Cys		525
	530	535
Gly Pro Leu Pro Asp Glu Pro Phe Ile Gln Met Ala Phe Leu Ser Leu		540
545	550	555
Pro Val Ile Pro Ala Leu Lys Leu Thr Ser Gln Gly Leu Phe Asp Gly		560
	565	570
Glu Lys Phe Ala Phe Thr Thr Leu Glu Val Thr Glu		575
	580	585

<210> 255

<211> 408

<212> PRT

<213> E. Coli

<400> 255

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Met Ala Tyr Cys Asn Pro Gly Leu Glu Ser Arg Pro Asn Lys Arg Asn
 1          5          10          15
Ala Leu Arg Arg His Val Val Thr Gly Ile Gly Met Lys Ile Val Ile
 20          25          30
Ala Pro Asp Ser Tyr Lys Glu Ser Leu Ser Ala Ser Glu Val Ala Gln
 35          40          45
Ala Ile Glu Lys Gly Phe Arg Glu Ile Phe Pro Asp Ala Gln Tyr Val
 50          55          60
Ser Val Pro Val Ala Asp Gly Gly Glu Gly Thr Val Glu Ala Met Ile
 65          70          75          80
Ala Ala Thr Gln Gly Ala Glu Arg His Ala Trp Val Thr Gly Pro Leu
 85          90          95
Gly Glu Lys Val Asn Ala Ser Trp Gly Ile Ser Gly Asp Gly Lys Thr
100          105          110
Ala Phe Ile Glu Met Ala Ala Ala Ser Gly Leu Glu Leu Val Pro Ala
115          120          125
Glu Lys Arg Asp Pro Leu Val Thr Thr Ser Arg Gly Thr Gly Glu Leu
130          135          140
Ile Leu Gln Ala Leu Glu Ser Gly Ala Thr Asn Ile Ile Ile Gly Ile
145          150          155          160
Gly Gly Ser Ala Thr Asn Asp Gly Gly Ala Gly Met Val Gln Ala Leu
165          170          175
Gly Ala Lys Leu Cys Asp Ala Asn Gly Asn Glu Ile Gly Phe Gly Gly
180          185          190
Gly Ser Leu Asn Thr Leu Asn Asp Ile Asp Ile Ser Gly Leu Asp Pro
195          200          205
Arg Leu Lys Asp Cys Val Ile Arg Val Ala Cys Asp Val Thr Asn Pro
210          215          220
Leu Val Gly Asp Asn Gly Ala Ser Arg Ile Phe Gly Pro Gln Lys Gly
225          230          235          240
Ala Ser Glu Ala Met Ile Val Glu Leu Asp Asn Asn Leu Ser His Tyr
245          250          255
Ala Glu Val Ile Lys Lys Ala Leu His Val Asp Val Lys Asp Val Pro
260          265          270
Gly Ala Gly Ala Ala Gly Gly Met Gly Ala Ala Leu Met Ala Phe Leu
275          280          285
Gly Ala Glu Leu Lys Ser Gly Ile Glu Ile Val Thr Thr Ala Leu Asn
290          295          300
Leu Glu Glu His Ile His Asp Cys Thr Leu Val Ile Thr Gly Glu Gly
305          310          315          320
Arg Ile Asp Ser Gln Ser Ile His Gly Lys Val Pro Ile Gly Val Ala
325          330          335
Asn Val Ala Lys Lys Tyr His Lys Pro Val Ile Gly Ile Ala Gly Ser
340          345          350
Leu Thr Asp Asp Val Gly Val Val His Gln His Gly Ile Asp Ala Val
355          360          365
Phe Ser Val Leu Thr Ser Ile Gly Thr Leu Asp Glu Ala Phe Arg Gly
370          375          380
Ala Tyr Asp Asn Ile Cys Arg Ala Ser Arg Asn Ile Ala Ala Thr Leu
385          390          395          400
Ala Ile Gly Met Arg Asn Ala Gly
405

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<210> 256

<211> 299

<212> PRT

<213> E. Coli

<400> 256

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Met Ile Asp Met Thr Met Lys Val Gly Phe Ile Gly Leu Gly Ile Met
 1           5           10           15
Gly Lys Pro Met Ser Lys Asn Leu Leu Lys Ala Gly Tyr Ser Leu Val
          20           25           30
Val Ala Asp Arg Asn Pro Glu Ala Ile Ala Asp Val Ile Ala Ala Gly
          35           40           45
Ala Glu Thr Ala Ser Thr Ala Lys Ala Ile Ala Glu Gln Cys Asp Val
 50           55           60
Ile Ile Thr Met Leu Pro Asn Ser Pro His Val Lys Glu Val Ala Leu
 65           70           75           80
Gly Glu Asn Gly Ile Ile Glu Gly Ala Lys Pro Gly Thr Val Leu Ile
          85           90           95
Asp Met Ser Ser Ile Ala Pro Leu Ala Ser Arg Glu Ile Ser Glu Ala
          100          105          110
Leu Lys Ala Lys Gly Ile Asp Met Leu Asp Ala Pro Val Ser Gly Gly
          115          120          125
Glu Pro Lys Ala Ile Asp Gly Thr Leu Ser Val Met Val Gly Gly Asp
 130          135          140
Lys Ala Ile Phe Asp Lys Tyr Tyr Asp Leu Met Lys Ala Met Ala Gly
 145          150          155          160
Ser Val Val His Thr Gly Glu Ile Gly Ala Gly Asn Val Thr Lys Leu
          165          170          175
Ala Asn Gln Val Ile Val Ala Leu Asn Ile Ala Ala Met Ser Glu Ala
          180          185          190
Leu Thr Leu Ala Thr Lys Ala Gly Val Asn Pro Asp Leu Val Tyr Gln
          195          200          205
Ala Ile Arg Gly Gly Leu Ala Gly Ser Thr Val Leu Asp Ala Lys Ala
 210          215          220
Pro Met Val Met Asp Arg Asn Phe Lys Pro Gly Phe Arg Ile Asp Leu
 225          230          235          240
His Ile Lys Asp Leu Ala Asn Ala Leu Asp Thr Ser His Gly Val Gly
          245          250          255
Ala Gln Leu Pro Leu Thr Ala Ala Val Met Glu Met Met Gln Ala Leu
          260          265          270
Arg Ala Asp Gly Leu Gly Thr Ala Asp His Ser Ala Leu Ala Cys Tyr
          275          280          285
Tyr Glu Lys Leu Ala Lys Val Glu Val Thr Arg
 290          295

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<210> 257

<211> 256

<212> PRT

<213> E. Coli

<400> 257

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Met Asn Asn Asp Val Phe Pro Asn Lys Phe Lys Ala Ala Leu Ala Ala
 1           5           10           15
Lys Gln Val Gln Ile Gly Cys Trp Ser Ala Leu Ser Asn Pro Ile Ser
          20           25           30
Thr Glu Val Leu Gly Leu Ala Gly Phe Asp Trp Leu Val Leu Asp Gly
          35           40           45
Glu His Ala Pro Asn Asp Ile Ser Thr Phe Ile Pro Gln Leu Met Ala
 50           55           60
Leu Lys Gly Ser Ala Ser Ala Pro Val Val Arg Val Pro Thr Asn Glu
 65           70           75           80
Pro Val Ile Ile Lys Arg Leu Leu Asp Ile Gly Phe Tyr Asn Phe Leu

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Ile	Pro	Phe	Val	85	Thr	Lys	Glu	90	Glu	Ala	Glu	Leu	Ala	95	Val	Ala	Ser
			100					105						110			
Thr	Arg	Tyr	Pro	Pro	Glu	Gly	Ile	Arg	Gly	Val	Ser	Val	Ser	His	Arg		
			115					120						125			
Ala	Asn	Met	Phe	Gly	Thr	Val	Ala	Asp	Tyr	Phe	Ala	Gln	Ser	Asn	Lys		
			130					135						140			
Asn	Ile	Thr	Ile	Leu	Val	Gln	Ile	Glu	Ser	Gln	Gln	Gly	Val	Asp	Asn		
						150					155				160		
Val	Asp	Ala	Ile	Ala	Ala	Thr	Glu	Gly	Val	Asp	Gly	Ile	Phe	Val	Gly		
						165					170				175		
Pro	Ser	Asp	Leu	Ala	Ala	Ala	Leu	Gly	His	Leu	Gly	Asn	Ala	Ser	His		
						180					185				190		
Pro	Asp	Val	Gln	Lys	Ala	Ile	Gln	His	Ile	Phe	Asn	Arg	Ala	Ser	Ala		
			195					200						205			
His	Gly	Lys	Pro	Ser	Gly	Ile	Leu	Ala	Pro	Val	Glu	Ala	Asp	Ala	Arg		
						210								220			
Arg	Tyr	Leu	Glu	Trp	Gly	Ala	Thr	Phe	Val	Ala	Val	Gly	Ser	Asp	Leu		
						225					235				240		
Gly	Val	Phe	Arg	Ser	Ala	Thr	Gln	Lys	Leu	Ala	Asp	Thr	Phe	Lys	Lys		
						245					250				255		

<210> 258

<211> 444

<212> PRT

<213> E. Coli

<400> 258

Met	Ile	Leu	Asp	Thr	Val	Asp	Glu	Lys	Lys	Lys	Gly	Val	His	Thr	Arg		
					5					10				15			
Tyr	Leu	Ile	Leu	Leu	Ile	Ile	Phe	Ile	Val	Thr	Ala	Val	Asn	Tyr	Ala		
										25				30			
Asp	Arg	Ala	Thr	Leu	Ser	Ile	Ala	Gly	Thr	Glu	Val	Ala	Lys	Glu	Leu		
										40				45			
Gln	Leu	Ser	Ala	Val	Ser	Met	Gly	Tyr	Ile	Phe	Ser	Ala	Phe	Gly	Trp		
														60			
Ala	Tyr	Leu	Leu	Met	Gln	Ile	Pro	Gly	Gly	Trp	Leu	Leu	Asp	Lys	Phe		
														80			
Gly	Ser	Lys	Lys	Val	Tyr	Thr	Tyr	Ser	Leu	Phe	Phe	Trp	Ser	Leu	Phe		
														95			
Thr	Phe	Leu	Gln	Gly	Phe	Val	Asp	Met	Phe	Pro	Leu	Ala	Trp	Ala	Gly		
														110			
Ile	Ser	Met	Phe	Phe	Met	Arg	Phe	Met	Leu	Gly	Phe	Ser	Glu	Ala	Pro		
														125			
Ser	Phe	Pro	Ala	Asn	Ala	Arg	Ile	Val	Ala	Ala	Trp	Phe	Pro	Thr	Lys		
														140			
Glu	Arg	Gly	Thr	Ala	Ser	Ala	Ile	Phe	Asn	Ser	Ala	Gln	Tyr	Phe	Ser		
														160			
Leu	Ala	Leu	Phe	Ser	Pro	Leu	Leu	Gly	Trp	Leu	Thr	Phe	Ala	Trp	Gly		
														175			
Trp	Glu	His	Val	Phe	Thr	Val	Met	Gly	Val	Ile	Gly	Phe	Val	Leu	Thr		
														190			
Ala	Leu	Trp	Ile	Lys	Leu	Ile	His	Asn	Pro	Thr	Asp	His	Pro	Arg	Met		
														205			
Ser	Ala	Glu	Glu	Leu	Lys	Phe	Ile	Ser	Glu	Asn	Gly	Ala	Val	Val	Asp		
														220			
Met	Asp	His	Lys	Lys	Pro	Gly	Ser	Ala	Ala	Ala	Ser	Gly	Pro	Lys	Leu		
														240			
His	Tyr	Ile	Lys	Gln	Leu	Leu	Ser	Asn	Arg	Met	Met	Leu	Gly	Val	Phe		
														255			

Phe	Gly	Gln	Tyr	Phe	Ile	Asn	Thr	Ile	Thr	Trp	Phe	Phe	Leu	Thr	Trp
			260					265					270		
Phe	Pro	Ile	Tyr	Leu	Val	Gln	Glu	Lys	Gly	Met	Ser	Ile	Leu	Lys	Val
		275					280					285			
Gly	Leu	Val	Ala	Ser	Ile	Pro	Ala	Leu	Cys	Gly	Phe	Ala	Gly	Gly	Val
	290					295					300				
Leu	Gly	Gly	Val	Phe	Ser	Asp	Tyr	Leu	Ile	Lys	Arg	Gly	Leu	Ser	Leu
305					310					315					320
Thr	Leu	Ala	Arg	Lys	Leu	Pro	Ile	Val	Leu	Gly	Met	Leu	Leu	Ala	Ser
				325					330					335	
Thr	Ile	Ile	Leu	Cys	Asn	Tyr	Thr	Asn	Asn	Thr	Thr	Leu	Val	Val	Met
			340					345					350		
Leu	Met	Ala	Leu	Ala	Phe	Phe	Gly	Lys	Gly	Phe	Gly	Ala	Leu	Gly	Trp
		355					360					365			
Pro	Val	Ile	Ser	Asp	Thr	Ala	Pro	Lys	Glu	Ile	Val	Gly	Leu	Cys	Gly
	370					375					380				
Gly	Val	Phe	Asn	Val	Phe	Gly	Asn	Val	Ala	Ser	Ile	Val	Thr	Pro	Leu
385					390					395					400
Val	Ile	Gly	Tyr	Leu	Val	Ser	Glu	Leu	His	Ser	Phe	Asn	Ala	Ala	Leu
			405						410					415	
Val	Phe	Val	Gly	Cys	Ser	Ala	Leu	Met	Ala	Met	Val	Cys	Tyr	Leu	Phe
			420					425					430		
Val	Val	Gly	Asp	Ile	Lys	Arg	Met	Glu	Leu	Gln	Lys				
		435					440								

<210> 259

<211> 511

<212> PRT

<213> E. Coli

<400> 259

Met 1	Gln	Thr	Ser	Asp 5	Thr	Arg	Ala	Leu	Pro 10	Leu	Leu	Cys	Ala	Arg 15	Ser
Val	Tyr	Lys	Gln 20	Tyr	Ser	Gly	Val	Asn 25	Val	Leu	Lys	Gly	Ile 30	Asp	Phe
Thr	Leu	His 35	Gln	Gly	Glu	Val	His 40	Ala	Leu	Leu	Gly	Gly 45	Asn	Gly	Ala
Gly	Lys	Ser	Thr	Leu	Met 50	Lys 55	Ile	Ile	Ala	Gly	Ile 60	Thr	Pro	Ala	Asp
Ser 65	Gly	Thr	Leu	Glu	Ile 70	Glu	Gly	Asn	Asn	Tyr 75	Val	Arg	Leu	Thr	Pro 80
Val	His	Ala	His 85	Gln	Leu	Gly	Ile	Tyr 90	Leu	Val	Pro	Gln	Glu 95	Pro	Leu
Leu	Phe	Pro	Ser 100	Leu	Ser	Ile	Lys 105	Glu	Asn	Ile	Leu	Phe 110	Gly	Leu	Ala
Lys	Lys	Gln 115	Leu	Ser	Met	Gln	Lys 120	Met	Lys	Asn	Leu	Leu 125	Ala	Ala	Leu
Gly	Cys	Gln	Phe	Asp	Leu	His 135	Ser	Leu	Ala	Gly	Ser 140	Leu	Asp	Val	Ala
Asp 145	Arg	Gln	Met	Val 150	Glu	Ile	Leu	Arg	Gly	Leu 155	Met	Arg	Asp	Ser	Arg 160
Ile	Leu	Ile	Leu	Asp 165	Glu	Pro	Thr	Ala	Ser	Leu 170	Thr	Pro	Ala 175	Glu	Thr
Glu	Arg	Leu	Phe 180	Ser	Arg	Leu	Gln 185	Glu	Leu	Leu	Ala	Thr 190	Gly	Val	Gly
Ile	Val	Phe 195	Ile	Ser	His	Lys	Leu 200	Pro	Glu	Ile	Arg	Gln 205	Ile	Ala	Asp
Arg	Ile	Ser	Val	Met	Arg	Asp 215	Gly	Thr	Ile	Ala	Leu 220	Ser	Gly	Lys	Thr
Ser	Glu	Leu	Ser	Thr	Asp	Asp	Ile	Ile	Gln	Ala	Ile	Thr	Pro	Ala	Val

225 230 235 240
 Arg Glu Lys Ser Leu Ser Ala Ser Gln Lys Leu Trp Leu Glu Leu Pro
 245 250 255
 Gly Asn Arg Pro Gln His Ala Ala Gly Thr Pro Val Leu Thr Leu Glu
 260 265 270
 Asn Leu Thr Gly Glu Gly Phe Arg Asn Val Ser Leu Thr Leu Asn Ala
 275 280 285
 Gly Glu Ile Leu Gly Leu Ala Gly Leu Val Gly Ala Gly Arg Thr Glu
 290 295 300
 Leu Ala Glu Thr Leu Tyr Gly Leu Arg Thr Leu Arg Gly Gly Arg Ile
 305 310 315 320
 Met Leu Asn Gly Lys Glu Ile Asn Lys Leu Ser Thr Gly Glu Arg Leu
 325 330 335
 Leu Arg Gly Leu Val Tyr Leu Pro Glu Asp Arg Gln Ser Ser Gly Leu
 340 345 350
 Asn Leu Asp Ala Ser Leu Ala Trp Asn Val Cys Ala Leu Thr His Asn
 355 360 365
 Leu Arg Gly Phe Trp Ala Lys Thr Ala Lys Asp Asn Ala Thr Leu Glu
 370 375 380
 Arg Tyr Arg Arg Ala Leu Asn Ile Lys Phe Asn Gln Pro Glu Gln Ala
 385 390 395 400
 Ala Arg Thr Leu Ser Gly Gly Asn Gln Gln Lys Ile Leu Ile Ala Lys
 405 410 415
 Cys Leu Glu Ala Ser Pro Gln Val Leu Ile Val Asp Glu Pro Thr Arg
 420 425 430
 Gly Val Asp Val Ser Ala Arg Asn Asp Ile Tyr Gln Leu Leu Arg Ser
 435 440 445
 Ile Ala Ala Gln Asn Val Ala Val Leu Leu Ile Ser Ser Asp Leu Glu
 450 455 460
 Glu Ile Glu Leu Met Ala Asp Arg Val Tyr Val Met His Gln Gly Glu
 465 470 475 480
 Ile Thr His Ser Ala Leu Thr Glu Arg Asp Ile Asn Val Glu Thr Ile
 485 490 495
 Met Arg Val Ala Phe Gly Asp Ser Gln Arg Gln Glu Ala Ser Cys
 500 505 510

<210> 260

<211> 342

<212> PRT

<213> E. Coli

<400> 260

Met Leu Lys Phe Ile Gln Asn Asn Arg Glu Ile Thr Ala Leu Leu Ala
 1 5 10 15
 Val Val Leu Leu Phe Val Leu Pro Gly Phe Leu Asp Arg Gln Tyr Leu
 20 25 30
 Ser Val Gln Thr Leu Thr Met Val Tyr Ser Ser Ala Gln Ile Leu Ile
 35 40 45
 Leu Leu Ala Met Gly Ala Thr Leu Val Met Leu Thr Arg Asn Ile Asp
 50 55 60
 Val Ser Val Gly Ser Ile Thr Gly Met Cys Ala Val Leu Leu Gly Met
 65 70 75 80
 Leu Leu Asn Ala Gly Tyr Ser Leu Pro Val Ala Cys Val Ala Thr Leu
 85 90 95
 Leu Leu Gly Leu Leu Ala Gly Phe Phe Asn Gly Val Leu Val Ala Trp
 100 105 110
 Leu Lys Ile Pro Ala Ile Val Ala Thr Leu Gly Thr Leu Gly Leu Tyr
 115 120 125
 Arg Gly Ile Met Leu Leu Trp Thr Gly Gly Lys Trp Ile Glu Gly Leu
 130 135 140

Pro Ala Glu Leu Lys Gln Leu Ser Ala Pro Leu Leu Leu Gly Val Ser
 145 150 155 160
 Ala Ile Gly Trp Leu Thr Ile Ile Leu Val Ala Phe Met Ala Trp Leu
 165 170 175
 Leu Ala Lys Thr Ala Phe Gly Arg Ser Phe Tyr Ala Thr Gly Asp Asn
 180 185 190
 Leu Gln Gly Ala Arg Gln Leu Gly Val Arg Thr Glu Ala Ile Arg Ile
 195 200 205
 Val Ala Phe Ser Leu Asn Gly Cys Met Ala Ala Leu Ala Gly Ile Val
 210 215 220
 Phe Ala Ser Gln Ile Gly Phe Ile Pro Asn Gln Thr Gly Thr Gly Leu
 225 230 235 240
 Glu Met Lys Ala Ile Ala Ala Cys Val Leu Gly Gly Ile Ser Leu Leu
 245 250 255
 Gly Gly Ser Gly Ala Ile Ile Gly Ala Val Leu Gly Ala Trp Phe Leu
 260 265 270
 Thr Gln Ile Asp Ser Val Leu Val Leu Leu Arg Ile Pro Ala Trp Trp
 275 280 285
 Asn Asp Phe Ile Ala Gly Leu Val Leu Leu Ala Val Leu Val Phe Asp
 290 295 300
 Gly Arg Leu Arg Cys Ala Leu Glu Arg Asn Leu Arg Arg Gln Lys Tyr
 305 310 315 320
 Ala Arg Phe Met Thr Pro Pro Pro Ser Val Lys Pro Ala Ser Ser Gly
 325 330 335
 Lys Lys Arg Glu Ala Ala
 340

<210> 261
 <211> 330
 <212> PRT
 <213> E. Coli

<400> 261
 Met Arg Ile Arg Tyr Gly Trp Glu Leu Ala Leu Ala Ala Leu Leu Val
 1 5 10 15
 Ile Glu Ile Val Ala Phe Gly Ala Ile Asn Pro Arg Met Leu Asp Leu
 20 25 30
 Asn Met Leu Leu Phe Ser Thr Ser Asp Phe Ile Cys Ile Gly Ile Val
 35 40 45
 Ala Leu Pro Leu Thr Met Val Ile Val Ser Gly Gly Ile Asp Ile Ser
 50 55 60
 Phe Gly Ser Thr Ile Gly Leu Cys Ala Ile Ala Leu Gly Val Leu Phe
 65 70 75 80
 Gln Ser Gly Val Pro Met Pro Leu Ala Ile Leu Leu Thr Leu Leu Leu
 85 90 95
 Gly Ala Leu Cys Gly Leu Ile Asn Ala Gly Leu Ile Ile Tyr Thr Lys
 100 105 110
 Val Asn Pro Leu Val Ile Thr Leu Gly Thr Leu Tyr Leu Phe Ala Gly
 115 120 125
 Ser Ala Leu Leu Leu Ser Gly Met Ala Gly Ala Thr Gly Tyr Glu Gly
 130 135 140
 Ile Gly Gly Phe Pro Met Ala Phe Thr Asp Phe Ala Asn Leu Asp Val
 145 150 155 160
 Leu Gly Leu Pro Val Pro Leu Ile Ile Phe Leu Ile Cys Leu Leu Val
 165 170 175
 Phe Trp Leu Trp Leu His Lys Thr His Ala Gly Arg Asn Val Phe Leu
 180 185 190
 Ile Gly Gln Ser Pro Arg Val Ala Leu Tyr Ser Ala Ile Pro Val Asn
 195 200 205
 Arg Thr Leu Cys Ala Leu Tyr Ala Met Thr Gly Leu Ala Ser Ala Val
 210 215 220

Ala Ala Val Leu Leu Val Ser Tyr Phe Gly Ser Ala Arg Ser Asp Leu
 225 230 235 240
 Gly Ala Ser Phe Leu Met Pro Ala Ile Thr Ala Val Val Leu Gly Gly
 245 250 255
 Ala Asn Ile Tyr Gly Gly Ser Gly Ser Ile Ile Gly Thr Ala Ile Ala
 260 265 270
 Val Leu Leu Val Gly Tyr Leu Gln Gln Gly Leu Gln Met Ala Gly Val
 275 280 285
 Pro Asn Gln Val Ser Ser Ala Leu Ser Gly Ala Leu Leu Ile Val Val
 290 295 300
 Val Val Gly Arg Ser Val Ser Leu His Arg Gln Gln Ile Lys Glu Trp
 305 310 315 320
 Leu Ala Arg Arg Ala Asn Asn Pro Leu Pro
 325 330

<210> 262

<211> 340

<212> PRT

<213> E. Coli

<400> 262

Met Thr Leu His Arg Phe Lys Lys Ile Ala Leu Leu Ser Ala Leu Gly
 1 5 10 15
 Ile Ala Ala Ile Ser Met Asn Val Gln Ala Ala Glu Arg Ile Ala Phe
 20 25 30
 Ile Pro Lys Leu Val Gly Val Gly Phe Phe Thr Ser Gly Gly Asn Gly
 35 40 45
 Ala Gln Gln Ala Gly Lys Glu Leu Gly Val Asp Val Thr Tyr Asp Gly
 50 55 60
 Pro Thr Glu Pro Ser Val Ser Gly Gln Val Gln Leu Ile Asn Asn Phe
 65 70 75 80
 Val Asn Gln Gly Tyr Asn Ala Ile Ile Val Ser Ala Val Ser Pro Asp
 85 90 95
 Gly Leu Cys Pro Ala Leu Lys Arg Ala Met Gln Arg Gly Val Arg Val
 100 105 110
 Leu Thr Trp Asp Ser Asp Thr Lys Pro Glu Cys Arg Ser Tyr Tyr Ile
 115 120 125
 Asn Gln Gly Thr Pro Ala Gln Leu Gly Gly Met Leu Val Asp Met Ala
 130 135 140
 Ala Arg Gln Val Asn Lys Asp Lys Ala Lys Val Ala Phe Phe Tyr Ser
 145 150 155 160
 Ser Pro Thr Val Thr Asp Gln Asn Gln Trp Val Lys Glu Ala Lys Ala
 165 170 175
 Lys Ile Ala Lys Glu His Pro Gly Trp Glu Ile Val Thr Thr Gln Phe
 180 185 190
 Gly Tyr Asn Asp Ala Thr Lys Ser Leu Gln Thr Ala Glu Gly Ile Leu
 195 200 205
 Lys Ala Tyr Ser Asp Leu Asp Ala Ile Ile Ala Pro Asp Ala Asn Ala
 210 215 220
 Leu Pro Ala Ala Ala Gln Ala Ala Glu Asn Leu Lys Asn Asp Lys Val
 225 230 235 240
 Ala Ile Val Gly Phe Ser Thr Pro Asn Val Met Arg Pro Tyr Val Glu
 245 250 255
 Arg Gly Thr Val Lys Glu Phe Gly Leu Trp Asp Val Val Gln Gln Gly
 260 265 270
 Lys Ile Ser Val Tyr Val Ala Asp Ala Leu Leu Lys Lys Gly Ser Met
 275 280 285
 Lys Thr Gly Asp Lys Leu Asp Ile Lys Gly Val Gly Gln Val Glu Val

290		295		300
Ser Pro Asn Ser Val	Gln Gly Tyr Asp Tyr	Glu Ala Asp Gly Asn Gly		
305	310	315		320
Ile Val Leu Leu Pro	Glu Arg Val Ile Phe Asn Lys Glu Asn Ile Gly			
	325	330		335
Lys Tyr Asp Phe				
	340			

<210> 263
 <211> 291
 <212> PRT
 <213> E. Coli

<400> 263
Met Ala Asp Leu Asp Asp Ile Lys Asp Gly Lys Asp Phe Arg Thr Asp
1 5 10 15
Gln Pro Gln Lys Asn Ile Pro Phe Thr Leu Lys Gly Cys Gly Ala Leu
20 25 30
Asp Trp Gly Met Gln Ser Arg Leu Ser Arg Ile Phe Asn Pro Lys Thr
35 40 45
Gly Lys Thr Val Met Leu Ala Phe Asp His Gly Tyr Phe Gln Gly Pro
50 55 60
Thr Thr Gly Leu Glu Arg Ile Asp Ile Asn Ile Ala Pro Leu Phe Glu
65 70 75 80
His Ala Asp Val Leu Met Cys Thr Arg Gly Ile Leu Arg Ser Val Val
85 90 95
Pro Pro Ala Thr Asn Arg Pro Val Val Leu Arg Ala Ser Gly Ala Asn
100 105 110
Ser Ile Leu Ala Glu Leu Ser Asn Glu Ala Val Ala Leu Ser Met Asp
115 120 125
Asp Ala Val Arg Leu Asn Ser Cys Ala Val Ala Ala Gln Val Tyr Ile
130 135 140
Gly Ser Glu Tyr Glu His Gln Ser Ile Lys Asn Ile Ile Gln Leu Val
145 150 155 160
Asp Ala Gly Met Lys Val Gly Met Pro Thr Met Ala Val Thr Gly Val
165 170 175
Gly Lys Asp Met Val Arg Asp Gln Arg Tyr Phe Ser Leu Ala Thr Arg
180 185 190
Ile Ala Ala Glu Met Gly Ala Gln Ile Ile Lys Thr Tyr Tyr Val Glu
195 200 205
Lys Gly Phe Glu Arg Ile Val Ala Gly Cys Pro Val Pro Ile Val Ile
210 215 220
Ala Gly Gly Lys Lys Leu Pro Glu Arg Glu Ala Leu Glu Met Cys Trp
225 230 235 240
Gln Ala Ile Asp Gln Gly Ala Ser Gly Val Asp Met Gly Arg Asn Ile
245 250 255
Phe Gln Ser Asp His Pro Val Ala Met Met Lys Ala Val Gln Ala Val
260 265 270
Val His His Asn Glu Thr Ala Asp Arg Ala Tyr Glu Leu Tyr Leu Ser
275 280 285
Glu Lys Gln
290

<210> 264
 <211> 96
 <212> PRT
 <213> E. Coli

<400> 264

Met His Val Thr Leu Val Glu Ile Asn Val His Glu Asp Lys Val Asp
 1 5 10 15
 Glu Phe Ile Glu Val Phe Arg Gln Asn His Leu Gly Ser Val Gln Glu
 20 25 30
 Glu Gly Asn Leu Arg Phe Asp Val Leu Gln Asp Pro Glu Val Asn Ser
 35 40 45
 Arg Phe Tyr Ile Tyr Glu Ala Tyr Lys Asp Glu Asp Ala Val Ala Phe
 50 55 60
 His Lys Thr Thr Pro His Tyr Lys Thr Cys Val Ala Lys Leu Glu Ser
 65 70 75 80
 Leu Met Thr Gly Pro Arg Lys Lys Arg Leu Phe Asn Gly Leu Met Pro
 85 90 95

<210> 265

<211> 383

<212> PRT

<213> E. Coli

<400> 265

Met Phe Glu Pro Met Glu Leu Thr Asn Asp Ala Val Ile Lys Val Ile
 1 5 10 15
 Gly Val Gly Gly Gly Gly Asn Ala Val Glu His Met Val Arg Glu
 20 25 30
 Arg Ile Glu Gly Val Glu Phe Phe Ala Val Asn Thr Asp Ala Gln Ala
 35 40 45
 Leu Arg Lys Thr Ala Val Gly Gln Thr Ile Gln Ile Gly Ser Gly Ile
 50 55 60
 Thr Lys Gly Leu Gly Ala Gly Ala Asn Pro Glu Val Gly Arg Asn Ala
 65 70 75 80
 Ala Asp Glu Asp Arg Asp Ala Leu Arg Ala Ala Leu Glu Gly Ala Asp
 85 90 95
 Met Val Phe Ile Ala Ala Gly Met Gly Gly Gly Thr Gly Thr Gly Ala
 100 105 110
 Ala Pro Val Val Ala Glu Val Ala Lys Asp Leu Gly Ile Leu Thr Val
 115 120 125
 Ala Val Val Thr Lys Pro Phe Asn Phe Glu Gly Lys Lys Arg Met Ala
 130 135 140
 Phe Ala Glu Gln Gly Ile Thr Glu Leu Ser Lys His Val Asp Ser Leu
 145 150 155 160
 Ile Thr Ile Pro Asn Asp Lys Leu Leu Lys Val Leu Gly Arg Gly Ile
 165 170 175
 Ser Leu Leu Asp Ala Phe Gly Ala Ala Asn Asp Val Leu Lys Gly Ala
 180 185 190
 Val Gln Gly Ile Ala Glu Leu Ile Thr Arg Pro Gly Leu Met Asn Val
 195 200 205
 Asp Phe Ala Asp Val Arg Thr Val Met Ser Glu Met Gly Tyr Ala Met
 210 215 220
 Met Gly Ser Gly Val Ala Ser Gly Glu Asp Arg Ala Glu Glu Ala Ala
 225 230 235 240
 Glu Met Ala Ile Ser Ser Pro Leu Leu Glu Asp Ile Asp Leu Ser Gly
 245 250 255
 Ala Arg Gly Val Leu Val Asn Ile Thr Ala Gly Phe Asp Leu Arg Leu
 260 265 270
 Asp Glu Phe Glu Thr Val Gly Asn Thr Ile Arg Ala Phe Ala Ser Asp
 275 280 285
 Asn Ala Thr Val Val Ile Gly Thr Ser Leu Asp Pro Asp Met Asn Asp
 290 295 300
 Glu Leu Arg Val Thr Val Val Ala Thr Gly Ile Gly Met Asp Lys Arg
 305 310 315 320
 Pro Glu Ile Thr Leu Val Thr Asn Lys Gln Val Gln Gln Pro Val Met

325 330 335
 Asp Arg Tyr Gln Gln His Gly Met Ala Pro Leu Thr Gln Glu Gln Lys
 340 345 350
 Pro Val Ala Lys Val Val Asn Asp Asn Ala Pro Gln Thr Ala Lys Glu
 355 360 365
 Pro Asp Tyr Leu Asp Ile Pro Ala Phe Leu Arg Lys Gln Ala Asp
 370 375 380

<210> 266
 <211> 1014
 <212> PRT
 <213> E. Coli

<400> 266
 Met Asp Val Ser Arg Arg Gln Phe Phe Lys Ile Cys Ala Gly Gly Met
 1 5 10 15
 Ala Gly Thr Thr Val Ala Ala Leu Gly Phe Ala Pro Lys Gln Ala Leu
 20 25 30
 Ala Gln Ala Arg Asn Tyr Lys Leu Leu Arg Ala Lys Glu Ile Arg Asn
 35 40 45
 Thr Cys Thr Tyr Cys Ser Val Gly Cys Gly Leu Leu Met Tyr Ser Leu
 50 55 60
 Gly Asp Gly Ala Lys Asn Ala Arg Glu Ala Ile Tyr His Ile Glu Gly
 65 70 75 80
 Asp Pro Asp His Pro Val Ser Arg Gly Ala Leu Cys Pro Lys Gly Ala
 85 90 95
 Gly Leu Leu Asp Tyr Val Asn Ser Glu Asn Arg Leu Arg Tyr Pro Glu
 100 105 110
 Tyr Arg Ala Pro Gly Ser Asp Lys Trp Gln Arg Ile Ser Trp Glu Glu
 115 120 125
 Ala Phe Ser Arg Ile Ala Lys Leu Met Lys Ala Asp Arg Asp Ala Asn
 130 135 140
 Phe Ile Glu Lys Asn Glu Gln Gly Val Thr Val Asn Arg Trp Leu Ser
 145 150 155 160
 Thr Gly Met Leu Cys Ala Ser Gly Ala Ser Asn Glu Thr Gly Met Leu
 165 170 175
 Thr Gln Lys Phe Ala Arg Ser Leu Gly Met Leu Ala Val Asp Asn Gln
 180 185 190
 Ala Arg Val His Gly Pro Thr Val Ala Ser Leu Ala Pro Thr Phe Gly
 195 200 205
 Arg Gly Ala Met Thr Asn His Trp Val Asp Ile Lys Asn Ala Asn Val
 210 215 220
 Val Met Val Met Gly Gly Asn Ala Ala Glu Ala His Pro Val Gly Phe
 225 230 235 240
 Arg Trp Ala Met Glu Ala Lys Asn Asn Asn Asp Ala Thr Leu Ile Val
 245 250 255
 Val Asp Pro Arg Phe Thr Arg Thr Ala Ser Val Ala Asp Ile Tyr Ala
 260 265 270
 Pro Ile Arg Ser Gly Thr Asp Ile Thr Phe Leu Ser Gly Val Leu Arg
 275 280 285
 Tyr Leu Ile Glu Asn Asn Lys Ile Asn Ala Glu Tyr Val Lys His Tyr
 290 295 300
 Thr Asn Ala Ser Leu Leu Val Arg Asp Asp Phe Ala Phe Glu Asp Gly
 305 310 315 320
 Leu Phe Ser Gly Tyr Asp Ala Glu Lys Arg Gln Tyr Asp Lys Ser Ser
 325 330 335
 Trp Asn Tyr Gln Leu Asp Glu Asn Gly Tyr Ala Lys Arg Asp Glu Thr
 340 345 350
 Leu Thr His Pro Arg Cys Val Trp Asn Leu Leu Lys Glu His Val Ser
 355 360 365

Arg Tyr Thr Pro Asp Val Val Glu Asn Ile Cys Gly Thr Pro Lys Ala
 370 375 380
 Asp Phe Leu Lys Val Cys Glu Val Leu Ala Ser Thr Ser Ala Pro Asp
 385 390 395 400
 Arg Thr Thr Thr Phe Leu Tyr Ala Leu Gly Trp Thr Gln His Thr Val
 405 410 415
 Gly Ala Gln Asn Ile Arg Thr Met Ala Met Ile Gln Leu Leu Leu Gly
 420 425 430
 Asn Met Gly Met Ala Gly Gly Gly Val Asn Ala Leu Arg Gly His Ser
 435 440 445
 Asn Ile Gln Gly Leu Thr Asp Leu Gly Leu Leu Ser Thr Ser Leu Pro
 450 455 460
 Gly Tyr Leu Thr Leu Pro Ser Glu Lys Gln Val Asp Leu Gln Ser Tyr
 465 470 475 480
 Leu Glu Ala Asn Thr Pro Lys Ala Thr Leu Ala Asp Gln Val Asn Tyr
 485 490 495
 Trp Ser Asn Tyr Pro Lys Phe Phe Val Ser Leu Met Lys Ser Phe Tyr
 500 505 510
 Gly Asp Ala Ala Gln Lys Glu Asn Asn Trp Gly Tyr Asp Trp Leu Pro
 515 520 525
 Lys Trp Asp Gln Thr Tyr Asp Val Ile Lys Tyr Phe Asn Met Met Asp
 530 535 540
 Glu Gly Lys Val Thr Gly Tyr Phe Cys Gln Gly Phe Asn Pro Val Ala
 545 550 555 560
 Ser Phe Pro Asp Lys Asn Lys Val Val Ser Cys Leu Ser Lys Leu Lys
 565 570 575
 Tyr Met Val Val Ile Asp Pro Leu Val Thr Glu Thr Ser Thr Phe Trp
 580 585 590
 Gln Asn His Gly Glu Ser Asn Asp Val Asp Pro Ala Ser Ile Gln Thr
 595 600 605
 Glu Val Phe Arg Leu Pro Ser Thr Cys Phe Ala Glu Glu Asp Gly Ser
 610 615 620
 Ile Ala Asn Ser Gly Arg Trp Leu Gln Trp His Trp Lys Gly Gln Asp
 625 630 635 640
 Ala Pro Gly Glu Ala Arg Asn Asp Gly Glu Ile Leu Ala Gly Ile Tyr
 645 650 655
 His His Leu Arg Glu Leu Tyr Gln Ser Glu Gly Gly Lys Gly Val Glu
 660 665 670
 Pro Leu Met Lys Met Ser Trp Asn Tyr Lys Gln Pro His Glu Pro Gln
 675 680 685
 Ser Asp Glu Val Ala Lys Glu Asn Asn Gly Tyr Ala Leu Glu Asp Leu
 690 695 700
 Tyr Asp Ala Asn Gly Val Leu Ile Ala Lys Lys Gly Gln Leu Leu Ser
 705 710 715 720
 Ser Phe Ala His Leu Arg Asp Asp Gly Thr Thr Ala Ser Ser Cys Trp
 725 730 735
 Ile Tyr Thr Gly Ser Trp Thr Glu Gln Gly Asn Gln Met Ala Asn Arg
 740 745 750
 Asp Asn Ser Asp Pro Ser Gly Leu Gly Asn Thr Leu Gly Trp Ala Trp
 755 760 765
 Ala Trp Pro Leu Asn Arg Arg Val Leu Tyr Asn Arg Ala Ser Ala Asp
 770 775 780
 Ile Asn Gly Lys Pro Trp Asp Pro Lys Arg Met Leu Ile Gln Trp Asn
 785 790 795 800
 Gly Ser Lys Trp Thr Gly Asn Asp Ile Pro Asp Phe Gly Asn Ala Ala
 805 810 815
 Pro Gly Thr Pro Thr Gly Pro Phe Ile Met Gln Pro Glu Gly Met Gly
 820 825 830
 Arg Leu Phe Ala Ile Asn Lys Met Ala Glu Gly Pro Phe Pro Glu His
 835 840 845
 Tyr Glu Pro Ile Glu Thr Pro Leu Gly Thr Asn Pro Leu His Pro Asn

850
 Val Val Ser Asn Pro Val Val Arg Leu Tyr Glu Gln Asp Ala Leu Arg
 865 870 875 880
 Met Gly Lys Lys Glu Gln Phe Pro Tyr Val Gly Thr Thr Tyr Arg Leu
 885 890 895
 Thr Glu His Phe His Thr Trp Thr Lys His Ala Leu Leu Asn Ala Ile
 900 905 910
 Ala Gln Pro Glu Gln Phe Val Glu Ile Ser Glu Thr Leu Ala Ala Ala
 915 920 925
 Lys Gly Ile Asn Asn Gly Asp Arg Val Thr Val Ser Ser Lys Arg Gly
 930 935 940
 Phe Ile Arg Ala Val Ala Val Val Thr Arg Arg Leu Lys Pro Leu Asn
 945 950 955 960
 Val Asn Gly Gln Gln Val Glu Thr Val Gly Ile Pro Ile His Trp Gly
 965 970 975
 Phe Glu Gly Val Ala Arg Lys Gly Tyr Ile Ala Asn Thr Leu Thr Pro
 980 985 990
 Asn Val Gly Asp Ala Asn Ser Gln Thr Pro Glu Tyr Lys Ala Phe Leu
 995 1000 1005
 Val Asn Ile Glu Lys Ala
 1010

<210> 267

<211> 294

<212> PRT

<213> E. Coli

<400> 267

Met Ala Met Glu Thr Gln Asp Ile Ile Lys Arg Ser Ala Thr Asn Ser
 1 5 10 15
 Ile Thr Pro Pro Ser Gln Val Arg Asp Tyr Lys Ala Glu Val Ala Lys
 20 25 30
 Leu Ile Asp Val Ser Thr Cys Ile Gly Cys Lys Ala Cys Gln Val Ala
 35 40 45
 Cys Ser Glu Trp Asn Asp Ile Arg Asp Glu Val Gly His Cys Val Gly
 50 55 60
 Val Tyr Asp Asn Pro Ala Asp Leu Ser Ala Lys Ser Trp Thr Val Met
 65 70 75 80
 Arg Phe Ser Glu Thr Glu Gln Asn Gly Lys Leu Glu Trp Leu Ile Arg
 85 90 95
 Lys Asp Gly Cys Met His Cys Glu Asp Pro Gly Cys Leu Lys Ala Cys
 100 105 110
 Pro Ser Ala Gly Ala Ile Ile Gln Tyr Ala Asn Gly Ile Val Asp Phe
 115 120 125
 Gln Ser Glu Asn Cys Ile Gly Cys Gly Tyr Cys Ile Ala Gly Cys Pro
 130 135 140
 Phe Asn Ile Pro Arg Leu Asn Lys Glu Asp Asn Arg Val Tyr Lys Cys
 145 150 155 160
 Thr Leu Cys Val Asp Arg Val Ser Val Gly Gln Glu Pro Ala Cys Val
 165 170 175
 Lys Thr Cys Pro Thr Gly Ala Ile His Phe Gly Thr Lys Lys Glu Met
 180 185 190
 Leu Glu Leu Ala Glu Gln Arg Val Ala Lys Leu Lys Ala Arg Gly Tyr
 195 200 205
 Glu His Ala Gly Val Tyr Asn Pro Glu Gly Val Gly Gly Thr His Val
 210 215 220
 Met Tyr Val Leu His His Ala Asp Gln Pro Glu Leu Tyr His Gly Leu
 225 230 235 240
 Pro Lys Asp Pro Lys Ile Asp Thr Ser Val Ser Leu Trp Lys Gly Ala
 245 250 255
 Leu Lys Pro Leu Ala Ala Ala Gly Phe Ile Ala Thr Phe Ala Gly Leu

260
 Ile Phe His Tyr Ile Gly Ile Gly Pro Asn Lys Glu Val Asp Asp Asp
 275 280 285
 Glu Glu Asp His His Glu
 290

<210> 268
 <211> 217
 <212> PRT
 <213> E. Coli

<400> 268
 Met Ser Lys Ser Lys Met Ile Val Arg Thr Lys Phe Ile Asp Arg Ala
 1 5 10 15
 Cys His Trp Thr Val Val Ile Cys Phe Leu Val Ala Leu Ser Gly
 20 25 30
 Ile Ser Phe Phe Phe Pro Thr Leu Gln Trp Leu Thr Gln Thr Phe Gly
 35 40 45
 Thr Pro Gln Met Gly Arg Ile Leu His Pro Phe Phe Gly Ile Ala Ile
 50 55 60
 Phe Val Ala Leu Met Phe Met Phe Val Arg Phe Val His His Asn Ile
 65 70 75 80
 Pro Asp Lys Lys Asp Ile Pro Trp Leu Leu Asn Ile Val Glu Val Leu
 85 90 95
 Lys Gly Asn Glu His Lys Val Ala Asp Val Gly Lys Tyr Asn Ala Gly
 100 105 110
 Gln Lys Met Met Phe Trp Ser Ile Met Ser Met Ile Phe Val Leu Leu
 115 120 125
 Val Thr Gly Val Ile Ile Trp Arg Pro Tyr Phe Ala Gln Tyr Phe Pro
 130 135 140
 Met Gln Val Val Arg Tyr Ser Leu Leu Ile His Ala Ala Ala Gly Ile
 145 150 155 160
 Ile Leu Ile His Ala Ile Leu Ile His Met Tyr Met Ala Phe Trp Val
 165 170 175
 Lys Gly Ser Ile Lys Gly Met Ile Glu Gly Lys Val Ser Arg Arg Trp
 180 185 190
 Ala Lys Lys His His Pro Arg Trp Tyr Arg Glu Ile Glu Lys Ala Glu
 195 200 205
 Ala Lys Lys Glu Ser Glu Glu Gly Ile
 210 215

<210> 269
 <211> 86
 <212> PRT
 <213> E. Coli

<400> 269
 Met Ala Leu Leu Ile Thr Lys Lys Cys Ile Asn Cys Asp Met Cys Glu
 1 5 10 15
 Pro Glu Cys Pro Asn Glu Ala Ile Ser Met Gly Asp His Ile Tyr Glu
 20 25 30
 Ile Asn Ser Asp Lys Cys Thr Glu Cys Val Gly His Tyr Glu Thr Pro
 35 40 45
 Thr Cys Gln Lys Val Cys Pro Ile Pro Asn Thr Ile Val Lys Asp Pro
 50 55 60
 Ala His Val Glu Thr Glu Glu Gln Leu Trp Asp Lys Phe Val Leu Met
 65 70 75 80
 His His Ala Asp Lys Ile
 85

<210> 270
 <211> 400
 <212> PRT
 <213> E. Coli

<400> 270
 Met Gln Ser Val Asp Val Ala Ile Val Gly Gly Gly Met Val Gly Leu
 1 5 10 15
 Ala Val Ala Cys Gly Leu Gln Gly Ser Gly Leu Arg Val Ala Val Leu
 20 25 30
 Glu Gln Arg Val Gln Glu Pro Leu Ala Ala Asn Ala Pro Pro Gln Leu
 35 40 45
 Arg Val Ser Ala Ile Asn Ala Ala Ser Glu Lys Leu Leu Thr Arg Leu
 50 55 60
 Gly Val Trp Gln Asp Ile Leu Ser Arg Arg Ala Ser Cys Tyr His Gly
 65 70 75 80
 Met Glu Val Trp Asp Lys Asp Ser Phe Gly His Ile Ser Phe Asp Asp
 85 90 95
 Gln Ser Met Gly Tyr Ser His Leu Gly His Ile Val Glu Asn Ser Val
 100 105 110
 Ile His Tyr Ala Leu Trp Asn Lys Ala His Gln Ser Ser Asp Ile Thr
 115 120 125
 Leu Leu Ala Pro Ala Glu Leu Gln Gln Val Ala Trp Gly Glu Asn Glu
 130 135 140
 Thr Phe Leu Thr Leu Lys Asp Gly Ser Met Leu Thr Ala Arg Leu Val
 145 150 155 160
 Ile Gly Ala Asp Gly Ala Asn Ser Trp Leu Arg Asn Lys Ala Asp Ile
 165 170 175
 Pro Leu Thr Phe Trp Asp Tyr Gln His His Ala Leu Val Ala Thr Ile
 180 185 190
 Arg Thr Glu Glu Pro His Asp Ala Val Ala Arg Gln Val Phe His Gly
 195 200 205
 Glu Gly Ile Leu Ala Phe Leu Pro Leu Ser Asp Pro His Leu Cys Ser
 210 215 220
 Ile Val Trp Ser Leu Ser Pro Glu Glu Ala Gln Arg Met Gln Gln Ala
 225 230 235 240
 Ser Glu Asp Glu Phe Asn Arg Ala Leu Asn Ile Ala Phe Asp Asn Arg
 245 250 255
 Leu Gly Leu Cys Lys Val Glu Ser Ala Arg Gln Val Phe Pro Leu Thr
 260 265 270
 Gly Arg Tyr Ala Arg Gln Phe Ala Ser His Arg Leu Ala Leu Val Gly
 275 280 285
 Asp Ala Ala His Thr Ile His Pro Leu Ala Gly Gln Gly Val Asn Leu
 290 295 300
 Gly Phe Met Asp Ala Ala Glu Leu Ile Ala Glu Leu Lys Arg Leu His
 305 310 315 320
 Arg Gln Gly Lys Asp Ile Gly Gln Tyr Ile Tyr Leu Arg Arg Tyr Glu
 325 330 335
 Arg Ser Arg Lys His Ser Ala Ala Leu Met Leu Ala Gly Met Gln Gly
 340 345 350
 Phe Arg Asp Leu Phe Ser Gly Thr Asn Pro Ala Lys Lys Leu Leu Arg
 355 360 365
 Asp Ile Gly Leu Lys Leu Ala Asp Thr Leu Pro Gly Val Lys Pro Gln
 370 375 380
 Leu Ile Arg Gln Ala Met Gly Leu Asn Asp Leu Pro Glu Trp Leu Arg
 385 390 395 400

<210> 271

<211> 392

<212> PRT

<213> E. Coli

<400> 271

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Met Ser Val Ile Ile Val Gly Gly Gly Met Ala Gly Ala Thr Leu Ala
 1          5          10          15
Leu Ala Ile Ser Arg Leu Ser His Gly Ala Leu Pro Val His Leu Ile
 20          25          30
Glu Ala Thr Ala Pro Glu Ser His Ala His Pro Gly Phe Asp Gly Arg
 35          40          45
Ala Ile Ala Leu Ala Ala Gly Thr Cys Gln Gln Leu Ala Arg Ile Gly
 50          55          60
Val Trp Gln Ser Leu Ala Asp Cys Ala Thr Ala Ile Thr Thr Val His
 65          70          75          80
Val Ser Asp Arg Gly His Ala Gly Phe Val Thr Leu Ala Ala Glu Asp
 85          90          95
Tyr Gln Leu Ala Ala Leu Gly Gln Val Val Glu Leu His Asn Val Gly
100          105          110
Gln Arg Leu Phe Ala Leu Leu Arg Lys Ala Pro Gly Val Thr Leu His
115          120          125
Cys Pro Asp Arg Val Ala Asn Val Ala Arg Thr Gln Ser His Val Glu
130          135          140
Val Thr Leu Glu Ser Gly Glu Thr Leu Thr Gly Arg Val Leu Val Ala
145          150          155          160
Ala Asp Gly Thr His Ser Ala Leu Ala Thr Ala Cys Gly Val Asp Trp
165          170          175
Gln Gln Glu Pro Tyr Glu Gln Leu Ala Val Ile Ala Asn Val Ala Thr
180          185          190
Ser Val Ala His Glu Gly Arg Ala Phe Glu Arg Phe Thr Gln His Gly
195          200          205
Pro Leu Ala Met Leu Pro Met Ser Asp Gly Arg Cys Ser Leu Val Trp
210          215          220
Cys His Pro Leu Glu Arg Arg Glu Glu Val Leu Ser Trp Ser Asp Glu
225          230          235          240
Lys Phe Cys Arg Glu Leu Gln Ser Ala Phe Gly Trp Arg Leu Gly Lys
245          250          255
Ile Thr His Ala Gly Lys Arg Ser Ala Tyr Pro Leu Ala Leu Thr His
260          265          270
Ala Ala Arg Ser Ile Thr His Arg Thr Val Leu Val Gly Asn Ala Ala
275          280          285
Gln Thr Leu His Pro Ile Ala Gly Gln Gly Phe Asn Leu Gly Met Arg
290          295          300
Asp Val Met Ser Leu Ala Glu Thr Leu Thr Gln Ala Gln Glu Arg Gly
305          310          315          320
Glu Asp Met Gly Asp Tyr Gly Val Leu Cys Arg Tyr Gln Gln Arg Arg
325          330          335
Gln Ser Asp Arg Glu Ala Thr Ile Gly Val Thr Asp Ser Leu Val His
340          345          350
Leu Phe Ala Asn Arg Trp Ala Pro Leu Val Val Gly Arg Asn Ile Gly
355          360          365
Leu Met Thr Met Glu Leu Phe Thr Pro Ala Arg Asp Val Leu Ala Gln
370          375          380
Arg Thr Leu Gly Trp Val Ala Arg
385          390

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<210> 272

<211> 441

<212> PRT

<213> E. Coli

<400> 272

Met	Ser	Glu	Ile	Ser	Arg	Gln	Glu	Phe	Gln	Arg	Arg	Arg	Gln	Ala	Leu
1				5					10					15	
Val	Glu	Gln	Met	Gln	Pro	Gly	Ser	Ala	Ala	Leu	Ile	Phe	Ala	Ala	Pro
			20					25					30		
Glu	Val	Thr	Arg	Ser	Ala	Asp	Ser	Glu	Tyr	Pro	Tyr	Arg	Gln	Asn	Ser
		35					40					45			
Asp	Phe	Trp	Tyr	Phe	Thr	Gly	Phe	Asn	Glu	Pro	Glu	Ala	Val	Leu	Val
	50					55					60				
Leu	Ile	Lys	Ser	Asp	Asp	Thr	His	Asn	His	Ser	Val	Leu	Phe	Asn	Arg
65				70						75					80
Val	Arg	Asp	Leu	Thr	Ala	Glu	Ile	Trp	Phe	Gly	Arg	Arg	Leu	Gly	Gln
				85					90					95	
Asp	Ala	Ala	Pro	Glu	Lys	Leu	Gly	Val	Asp	Arg	Ala	Leu	Ala	Phe	Ser
			100					105					110		
Glu	Ile	Asn	Gln	Gln	Leu	Tyr	Gln	Leu	Leu	Asn	Gly	Leu	Asp	Val	Val
		115					120					125			
Tyr	His	Ala	Gln	Gly	Glu	Tyr	Ala	Tyr	Ala	Asp	Val	Ile	Val	Asn	Ser
	130					135					140				
Ala	Leu	Glu	Lys	Leu	Arg	Lys	Gly	Ser	Arg	Gln	Asn	Leu	Thr	Ala	Pro
145					150					155					160
Ala	Thr	Met	Ile	Asp	Trp	Arg	Pro	Val	Val	His	Glu	Met	Arg	Leu	Phe
				165					170					175	
Lys	Ser	Pro	Glu	Glu	Ile	Ala	Val	Leu	Arg	Arg	Ala	Gly	Glu	Ile	Thr
			180					185					190		
Ala	Met	Ala	His	Thr	Arg	Ala	Met	Glu	Lys	Cys	Arg	Pro	Gly	Met	Phe
	195						200					205			
Glu	Tyr	His	Leu	Glu	Gly	Glu	Ile	His	His	Glu	Phe	Asn	Arg	His	Gly
	210					215					220				
Ala	Arg	Tyr	Pro	Ser	Tyr	Asn	Thr	Ile	Val	Gly	Ser	Gly	Glu	Asn	Gly
225					230					235					240
Cys	Ile	Leu	His	Tyr	Thr	Glu	Asn	Glu	Cys	Glu	Met	Arg	Asp	Gly	Asp
				245					250					255	
Leu	Val	Leu	Ile	Asp	Ala	Gly	Cys	Glu	Tyr	Lys	Gly	Tyr	Ala	Gly	Asp
			260					265					270		
Ile	Thr	Arg	Thr	Phe	Pro	Val	Asn	Gly	Lys	Phe	Thr	Gln	Ala	Gln	Arg
			275				280					285			
Glu	Ile	Tyr	Asp	Ile	Val	Leu	Glu	Ser	Leu	Glu	Thr	Ser	Leu	Arg	Leu
	290					295					300				
Tyr	Arg	Pro	Gly	Thr	Ser	Ile	Leu	Glu	Val	Thr	Gly	Glu	Val	Val	Arg
305					310					315					320
Ile	Met	Val	Ser	Gly	Leu	Val	Lys	Leu	Gly	Ile	Leu	Lys	Gly	Asp	Val
				325					330					335	
Asp	Glu	Leu	Ile	Ala	Gln	Asn	Ala	His	Arg	Pro	Phe	Phe	Met	His	Gly
			340					345					350		
Leu	Ser	His	Trp	Leu	Gly	Leu	Asp	Val	His	Asp	Val	Gly	Val	Tyr	Gly
			355				360					365			
Gln	Asp	Arg	Ser	Arg	Ile	Leu	Glu	Pro	Gly	Met	Val	Leu	Thr	Val	Glu
	370					375					380				
Pro	Gly	Leu	Tyr	Ile	Ala	Pro	Asp	Ala	Glu	Val	Pro	Glu	Gln	Tyr	Arg
385					390					395					400
Gly	Ile	Gly	Ile	Arg	Ile	Glu	Asp	Asp	Ile	Val	Ile	Thr	Glu	Thr	Gly
				405					410					415	
Asn	Glu	Asn	Leu	Thr	Ala	Ser	Val	Val	Lys	Lys	Pro	Glu	Glu	Ile	Glu
			420					425					430		
Ala	Leu	Met	Val	Ala	Ala	Arg	Lys	Gln							
			435				440								

<210> 273

<211> 194
 <212> PRT
 <213> E. Coli

<400> 273
 Met Leu Met Ser Ile Gln Asn Glu Met Pro Gly Tyr Asn Glu Met Asn
 1 5 10 15
 Gln Tyr Leu Asn Gln Gln Gly Thr Gly Leu Thr Pro Ala Glu Met His
 20 25 30
 Gly Leu Ile Ser Gly Met Ile Cys Gly Gly Asn Asp Asp Ser Ser Trp
 35 40 45
 Leu Pro Leu Leu His Asp Leu Thr Asn Glu Gly Met Ala Phe Gly His
 50 55 60
 Glu Leu Ala Gln Ala Leu Arg Lys Met His Ser Ala Thr Ser Asp Ala
 65 70 75 80
 Leu Gln Asp Asp Gly Phe Leu Phe Gln Leu Tyr Leu Pro Asp Gly Asp
 85 90 95
 Asp Val Ser Val Phe Asp Arg Ala Asp Ala Leu Ala Gly Trp Val Asn
 100 105 110
 His Phe Leu Leu Gly Leu Gly Val Thr Gln Pro Lys Leu Asp Lys Val
 115 120 125
 Thr Gly Glu Thr Gly Glu Ala Ile Asp Asp Leu Arg Asn Ile Ala Gln
 130 135 140
 Leu Gly Tyr Asp Glu Asp Glu Asp Gln Glu Glu Leu Glu Met Ser Leu
 145 150 155 160
 Glu Glu Ile Ile Glu Tyr Val Arg Val Ala Ala Leu Leu Cys His Asp
 165 170 175
 Thr Phe Thr His Pro Gln Pro Thr Ala Pro Glu Val Gln Lys Pro Thr
 180 185 190
 Leu His

<210> 274
 <211> 120
 <212> PRT
 <213> E. Coli

<400> 274
 Met Leu Lys Leu Phe Ala Lys Tyr Thr Ser Ile Gly Val Leu Asn Thr
 1 5 10 15
 Leu Ile His Trp Val Val Phe Gly Val Cys Ile Tyr Val Ala His Thr
 20 25 30
 Asn Gln Ala Leu Ala Asn Phe Ala Gly Phe Val Val Ala Val Ser Phe
 35 40 45
 Ser Phe Phe Ala Asn Ala Lys Phe Thr Phe Lys Ala Ser Thr Thr Thr
 50 55 60
 Met Arg Tyr Met Leu Tyr Val Gly Phe Met Gly Thr Leu Ser Ala Thr
 65 70 75 80
 Val Gly Trp Ala Ala Asp Arg Cys Ala Leu Pro Pro Met Ile Thr Leu
 85 90 95
 Val Thr Phe Ser Ala Ile Ser Leu Val Cys Gly Phe Val Tyr Ser Lys
 100 105 110
 Phe Ile Val Phe Arg Asp Ala Lys
 115 120

<210> 275
 <211> 306
 <212> PRT
 <213> E. Coli

<400> 275

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Met Lys Ile Ser Leu Val Val Pro Val Phe Asn Glu Glu Glu Ala Ile
 1      5      10      15
Pro Ile Phe Tyr Lys Thr Val Arg Glu Phe Glu Glu Leu Lys Ser Tyr
      20      25      30
Glu Val Glu Ile Val Phe Ile Asn Asp Gly Ser Lys Asp Ala Thr Glu
      35      40      45
Ser Ile Ile Asn Ala Leu Ala Val Ser Asp Pro Leu Val Val Pro Leu
      50      55      60
Ser Phe Thr Arg Asn Phe Gly Lys Glu Pro Ala Leu Phe Ala Gly Leu
      65      70      75      80
Asp His Ala Thr Gly Asp Ala Ile Ile Pro Ile Asp Val Asp Leu Gln
      85      90      95
Asp Pro Ile Glu Val Ile Pro His Leu Ile Glu Lys Trp Gln Ala Gly
      100      105      110
Ala Asp Met Val Leu Ala Lys Arg Ser Asp Arg Ser Thr Asp Gly Arg
      115      120      125
Leu Lys Arg Lys Thr Ala Glu Trp Phe Tyr Lys Leu His Asn Lys Ile
      130      135      140
Ser Asn Pro Lys Ile Glu Glu Asn Val Gly Asp Phe Arg Leu Met Ser
      145      150      155      160
Arg Asp Val Val Glu Asn Ile Lys Leu Met Pro Glu Arg Asn Leu Phe
      165      170      175
Met Lys Gly Ile Leu Ser Trp Val Gly Gly Lys Thr Asp Ile Val Glu
      180      185      190
Tyr Val Arg Ala Glu Arg Ile Ala Gly Asp Thr Lys Phe Asn Gly Trp
      195      200      205
Lys Leu Trp Asn Leu Ala Leu Glu Gly Ile Thr Ser Phe Ser Thr Phe
      210      215      220
Pro Leu Arg Ile Trp Thr Tyr Ile Gly Leu Val Val Ala Ser Val Ala
      225      230      235      240
Phe Ile Tyr Gly Ala Trp Met Ile Leu Asp Thr Ile Ile Phe Gly Asn
      245      250      255
Ala Val Arg Gly Tyr Pro Ser Leu Leu Val Ser Ile Leu Phe Leu Gly
      260      265      270
Gly Ile Gln Met Ile Gly Ile Gly Val Leu Gly Glu Tyr Ile Gly Arg
      275      280      285
Thr Tyr Ile Glu Thr Lys Lys Arg Pro Lys Tyr Ile Ile Lys Arg Val
      290      295      300
Lys Lys
305

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<210> 276

<211> 443

<212> PRT

<213> E. Coli

<400> 276

```

Met Asn Lys Ala Ile Lys Val Ser Leu Tyr Ile Ser Phe Val Leu Ile
 1      5      10      15
Ile Cys Ala Leu Ser Lys Asn Ile Met Met Leu Asn Thr Ser Asp Phe
      20      25      30
Gly Arg Ala Ile Lys Pro Leu Ile Glu Asp Ile Pro Ala Phe Thr Tyr
      35      40      45
Asp Leu Pro Leu Leu Tyr Lys Leu Lys Gly His Ile Asp Ser Ile Asp
      50      55      60
Ser Tyr Glu Tyr Ile Ser Ser Tyr Ser Tyr Ile Leu Tyr Thr Tyr Val
      65      70      75      80
Leu Phe Ile Ser Ile Phe Thr Glu Tyr Leu Asp Ala Arg Val Leu Ser
      85      90      95

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Leu Phe Leu Lys Val Ile Tyr Ile Tyr Ser Leu Tyr Ala Ile Phe Thr
 100 105 110
 Ser Tyr Ile Lys Thr Glu Arg Tyr Val Thr Leu Phe Thr Phe Phe Ile
 115 120 125
 Leu Ala Phe Leu Met Cys Ser Ser Ser Thr Leu Ser Met Phe Ala Ser
 130 135 140
 Phe Tyr Gln Glu Gln Ile Val Ile Ile Phe Leu Pro Phe Leu Val Tyr
 145 150 155 160
 Ser Leu Thr Cys Lys Asn Asn Lys Ser Met Leu Leu Leu Phe Phe Ser
 165 170 175
 Leu Leu Ile Ile Ser Thr Ala Lys Asn Gln Phe Ile Leu Thr Pro Leu
 180 185 190
 Ile Val Tyr Ser Tyr Tyr Ile Phe Phe Asp Arg His Lys Leu Ile Ile
 195 200 205
 Lys Ser Val Ile Cys Val Val Cys Leu Leu Ala Ser Ile Phe Ala Ile
 210 215 220
 Ser Tyr Ser Lys Gly Val Val Glu Leu Asn Lys Tyr His Ala Thr Tyr
 225 230 235 240
 Phe Gly Ser Tyr Leu Tyr Met Lys Asn Asn Gly Tyr Lys Met Pro Ser
 245 250 255
 Tyr Val Asp Asp Lys Cys Val Gly Leu Asp Ala Trp Gly Asn Lys Phe
 260 265 270
 Asp Ile Ser Phe Gly Ala Thr Pro Thr Glu Val Gly Thr Glu Cys Phe
 275 280 285
 Glu Ser His Lys Asp Glu Thr Phe Ser Asn Ala Leu Phe Leu Leu Val
 290 295 300
 Ser Lys Pro Ser Thr Ile Phe Lys Leu Pro Phe Asp Asp Gly Val Met
 305 310 315 320
 Ser Gln Tyr Lys Glu Asn Tyr Phe His Val Tyr Lys Lys Leu His Val
 325 330 335
 Ile Tyr Gly Glu Ser Asn Ile Leu Thr Thr Ile Thr Asn Ile Lys Asp
 340 345 350
 Asn Ile Phe Lys Asn Ile Arg Phe Ile Ser Leu Leu Leu Phe Phe Ile
 355 360 365
 Ala Ser Ile Phe Ile Arg Asn Asn Lys Ile Lys Ala Ser Leu Phe Val
 370 375 380
 Val Ser Leu Phe Gly Ile Ser Gln Phe Tyr Val Ser Phe Phe Gly Glu
 385 390 395 400
 Gly Tyr Arg Asp Leu Ser Lys His Leu Phe Gly Met Tyr Phe Ser Phe
 405 410 415
 Asp Leu Cys Leu Tyr Ile Thr Val Val Phe Leu Ile Tyr Lys Ile Ile
 420 425 430
 Gln Arg Asn Gln Asp Asn Ser Asp Val Lys His
 435 440

<210> 277

<211> 82

<212> PRT

<213> E. Coli

<400> 277

Met Gly Ile Leu Ser Trp Ile Ile Phe Gly Leu Ile Ala Gly Ile Leu
 1 5 10 15
 Ala Lys Trp Ile Met Pro Gly Lys Asp Gly Gly Gly Phe Phe Met Thr
 20 25 30
 Ile Leu Leu Gly Ile Val Gly Ala Val Val Gly Gly Trp Ile Ser Thr
 35 40 45
 Leu Phe Gly Phe Gly Lys Val Asp Gly Phe Asn Phe Gly Ser Phe Val
 50 55 60

Val Ala Val Ile Gly Ala Ile Val Val Leu Phe Ile Tyr Arg Lys Ile
 65 70 75 80
 Lys Ser

<210> 278
 <211> 60
 <212> PRT
 <213> E. Coli

<400> 278
 Met Gly Lys Ala Thr Tyr Thr Val Thr Val Thr Asn Asn Ser Asn Gly
 1 5 10 15
 Val Ser Val Asp Tyr Glu Thr Glu Thr Pro Met Thr Leu Leu Val Pro
 20 25 30
 Glu Val Ala Ala Glu Val Ile Lys Asp Leu Val Asn Thr Val Arg Ser
 35 40 45
 Tyr Asp Thr Glu Asn Glu His Asp Val Cys Gly Trp
 50 55 60

<210> 279
 <211> 119
 <212> PRT
 <213> E. Coli

<400> 279
 Met Leu Gln Ile Pro Gln Asn Tyr Ile His Thr Arg Ser Thr Pro Phe
 1 5 10 15
 Trp Asn Lys Gln Thr Ala Pro Ala Gly Ile Phe Glu Arg His Leu Asp
 20 25 30
 Lys Gly Thr Arg Pro Gly Val Tyr Pro Arg Leu Ser Val Met His Gly
 35 40 45
 Ala Val Lys Tyr Leu Gly Tyr Ala Asp Glu His Ser Ala Glu Pro Asp
 50 55 60
 Gln Val Ile Leu Ile Glu Ala Gly Gln Phe Ala Val Phe Pro Pro Glu
 65 70 75 80
 Lys Trp His Asn Ile Glu Ala Met Thr Asp Asp Thr Tyr Phe Asn Ile
 85 90 95
 Asp Phe Phe Val Ala Pro Glu Val Leu Met Glu Gly Ala Gln Gln Arg
 100 105 110
 Lys Val Ile His Asn Gly Lys
 115

<210> 280
 <211> 246
 <212> PRT
 <213> E. Coli

<400> 280
 Met Lys Phe Lys Val Ile Ala Leu Ala Ala Leu Met Gly Ile Ser Gly
 1 5 10 15
 Met Ala Ala Gln Ala Asn Glu Leu Pro Asp Gly Pro His Ile Val Thr
 20 25 30
 Ser Gly Thr Ala Ser Val Asp Ala Val Pro Asp Ile Ala Thr Leu Ala
 35 40 45
 Ile Glu Val Asn Val Ala Ala Lys Asp Ala Ala Thr Ala Lys Lys Gln
 50 55 60
 Ala Asp Glu Arg Val Ala Gln Tyr Ile Ser Phe Leu Glu Leu Asn Gln


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65          70          75          80
Ile Ala Lys Lys Asp Ile Ser Ser Ala Asn Leu Arg Thr Gln Pro Asp
      85          90
Tyr Asp Tyr Gln Asp Gly Lys Ser Ile Leu Lys Gly Tyr Arg Ala Val
      100          105          110
Arg Thr Val Glu Val Thr Leu Arg Gln Leu Asp Lys Leu Asn Ser Leu
      115          120          125
Leu Asp Gly Ala Leu Lys Ala Gly Leu Asn Glu Ile Arg Ser Val Ser
      130          135          140
Leu Gly Val Ala Gln Pro Asp Ala Tyr Lys Asp Lys Ala Arg Lys Ala
      145          150          155          160
Ala Ile Asp Asn Ala Ile His Gln Ala Gln Glu Leu Ala Asn Gly Phe
      165          170          175
His Arg Lys Leu Gly Pro Val Tyr Ser Val Arg Tyr His Val Ser Asn
      180          185          190
Tyr Gln Pro Ser Pro Met Val Arg Met Met Lys Ala Asp Ala Ala Pro
      195          200          205
Val Ser Ala Gln Glu Thr Tyr Glu Gln Ala Ala Ile Gln Phe Asp Asp
      210          215          220
Gln Val Asp Val Val Phe Gln Leu Glu Pro Val Asp Gln Gln Pro Ala
      225          230          235          240
Lys Thr Pro Ala Ala Gln
      245

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<210> 281
 <211> 464
 <212> PRT
 <213> E. Coli

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<400> 281
Met Leu Leu Leu Asp Ala Cys Ser Gln Met Cys Pro Ser Phe Arg Arg
  1          5          10          15
Phe Gln Thr Val Phe His Asn Ser Ser Ile Phe Leu Pro Tyr Trp Leu
      20          25          30
Ala Thr Leu Val Ser Phe Arg Glu Thr Phe Gln Glu Glu Lys Leu Leu
      35          40          45
Thr Met Lys Gly Ser Tyr Lys Ser Arg Trp Val Ile Val Ile Val Val
      50          55          60
Val Ile Ala Ala Ile Ala Ala Phe Trp Phe Trp Gln Gly Arg Asn Asp
      65          70          75          80
Ser Arg Ser Ala Ala Pro Gly Ala Thr Lys Gln Ala Gln Gln Ser Pro
      85          90          95
Ala Gly Gly Arg Arg Gly Met Arg Ser Gly Pro Leu Ala Pro Val Gln
      100          105          110
Ala Ala Thr Ala Val Glu Gln Ala Val Pro Arg Tyr Leu Thr Gly Leu
      115          120          125
Gly Thr Ile Thr Ala Ala Asn Thr Val Thr Val Arg Ser Arg Val Asp
      130          135          140
Gly Gln Leu Ile Ala Leu His Phe Gln Glu Gly Gln Gln Val Lys Ala
      145          150          155          160
Gly Asp Leu Leu Ala Glu Ile Asp Pro Ser Gln Phe Lys Val Ala Leu
      165          170          175
Ala Gln Ala Gln Gly Gln Leu Ala Lys Asp Lys Ala Thr Leu Ala Asn
      180          185          190
Ala Arg Arg Asp Leu Ala Arg Tyr Gln Gln Leu Ala Lys Thr Asn Leu
      195          200          205
Val Ser Arg Gln Glu Leu Asp Ala Gln Gln Ala Leu Val Ser Glu Thr
      210          215          220
Glu Gly Thr Ile Lys Ala Asp Glu Ala Ser Val Ala Ser Ala Gln Leu
      225          230          235          240

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Gln Leu Asp Trp Ser Arg Ile Thr Ala Pro Val Asp Gly Arg Val Gly
 245 250 255
 Leu Lys Gln Val Asp Val Gly Asn Gln Ile Ser Ser Gly Asp Thr Thr
 260 265 270
 Gly Ile Val Val Ile Thr Gln Thr His Pro Ile Asp Leu Val Phe Thr
 275 280 285
 Leu Pro Glu Ser Asp Ile Ala Thr Val Val Gln Ala Gln Lys Ala Gly
 290 295 300
 Lys Pro Leu Val Val Glu Ala Trp Asp Arg Thr Asn Ser Lys Lys Leu
 305 310 315 320
 Ser Glu Gly Thr Leu Leu Ser Leu Asp Asn Gln Ile Asp Ala Thr Thr
 325 330 335
 Gly Thr Ile Lys Val Lys Ala Arg Phe Asn Asn Gln Asp Asp Ala Leu
 340 345 350
 Phe Pro Asn Gln Phe Val Asn Ala Arg Met Leu Val Asp Thr Glu Gln
 355 360 365
 Asn Ala Val Val Ile Pro Thr Ala Ala Leu Gln Met Gly Asn Glu Gly
 370 375 380
 His Phe Val Trp Val Leu Asn Ser Glu Asn Lys Val Ser Lys His Leu
 385 390 395 400
 Val Thr Pro Gly Ile Gln Asp Ser Gln Lys Val Val Ile Arg Ala Gly
 405 410 415
 Ile Ser Ala Gly Asp Arg Val Val Thr Asp Gly Ile Asp Arg Leu Thr
 420 425 430
 Glu Gly Ala Lys Val Glu Val Val Glu Ala Gln Ser Ala Thr Thr Pro
 435 440 445
 Glu Glu Lys Ala Thr Ser Arg Glu Tyr Ala Lys Lys Gly Ala Arg Ser
 450 455 460

<210> 282

<211> 1040

<212> PRT

<213> E. Coli

<400> 282

Met Gln Val Leu Pro Pro Ser Ser Thr Gly Gly Pro Ser Arg Leu Phe
 1 5 10 15
 Ile Met Arg Pro Val Ala Thr Thr Leu Met Val Ala Ile Leu Leu
 20 25 30
 Ala Gly Ile Ile Gly Tyr Arg Ala Leu Pro Val Ser Ala Leu Pro Glu
 35 40 45
 Val Asp Tyr Pro Thr Ile Gln Val Val Thr Leu Tyr Pro Gly Ala Ser
 50 55 60
 Pro Asp Val Met Thr Ser Ala Val Thr Ala Pro Leu Glu Arg Gln Phe
 65 70 75 80
 Gly Gln Met Ser Gly Leu Lys Gln Met Ser Ser Gln Ser Ser Gly Gly
 85 90 95
 Ala Ser Val Ile Thr Leu Gln Phe Gln Leu Thr Leu Pro Leu Asp Val
 100 105 110
 Ala Glu Gln Glu Val Gln Ala Ala Ile Asn Ala Ala Thr Asn Leu Leu
 115 120 125
 Pro Ser Asp Leu Pro Asn Pro Pro Val Tyr Ser Lys Val Asn Pro Ala
 130 135 140
 Asp Pro Pro Ile Met Thr Leu Ala Val Thr Ser Thr Ala Met Pro Met
 145 150 155 160
 Thr Gln Val Glu Asp Met Val Glu Thr Arg Val Ala Gln Lys Ile Ser
 165 170 175
 Gln Ile Ser Gly Val Gly Leu Val Thr Leu Ser Gly Gly Gln Arg Pro
 180 185 190
 Ala Val Arg Val Lys Leu Asn Ala Gln Ala Ile Ala Ala Leu Gly Leu

195					200					205					
Thr	Ser	Glu	Thr	Val	Arg	Thr	Ala	Ile	Thr	Gly	Ala	Asn	Val	Asn	Ser
210						215					220				
Ala	Lys	Gly	Ser	Leu	Asp	Gly	Pro	Ser	Arg	Ala	Val	Thr	Leu	Ser	Ala
225					230					235					240
Asn	Asp	Gln	Met	Gln	Ser	Ala	Glu	Glu	Tyr	Arg	Gln	Leu	Ile	Ile	Ala
				245					250					255	
Tyr	Gln	Asn	Gly	Ala	Pro	Ile	Arg	Leu	Gly	Asp	Val	Ala	Thr	Val	Glu
			260					265					270		
Gln	Gly	Ala	Glu	Asn	Ser	Trp	Leu	Gly	Ala	Trp	Ala	Asn	Lys	Glu	Gln
		275					280					285			
Ala	Ile	Val	Met	Asn	Val	Gln	Arg	Gln	Pro	Gly	Ala	Asn	Ile	Ile	Ser
290						295					300				
Thr	Ala	Asp	Ser	Ile	Arg	Gln	Met	Leu	Pro	Gln	Leu	Thr	Glu	Ser	Leu
305				310						315					320
Pro	Lys	Ser	Val	Lys	Val	Thr	Val	Leu	Ser	Asp	Arg	Thr	Thr	Asn	Ile
				325					330					335	
Arg	Ala	Ser	Val	Asp	Asp	Thr	Gln	Phe	Glu	Leu	Met	Met	Ala	Ile	Ala
			340					345					350		
Leu	Val	Val	Met	Ile	Ile	Tyr	Leu	Phe	Leu	Arg	Asn	Ile	Pro	Ala	Thr
		355					360					365			
Ile	Ile	Pro	Gly	Val	Ala	Val	Pro	Leu	Ser	Leu	Ile	Gly	Thr	Phe	Ala
370						375					380				
Val	Met	Val	Phe	Leu	Asp	Phe	Ser	Ile	Asn	Asn	Leu	Thr	Leu	Met	Ala
385				390					395						400
Leu	Thr	Ile	Ala	Thr	Gly	Phe	Val	Val	Asp	Asp	Ala	Ile	Val	Val	Ile
				405					410					415	
Glu	Asn	Ile	Ser	Arg	Tyr	Ile	Glu	Lys	Gly	Glu	Lys	Pro	Leu	Ala	Ala
			420					425					430		
Ala	Leu	Lys	Gly	Ala	Gly	Glu	Ile	Gly	Phe	Thr	Ile	Ile	Ser	Leu	Thr
		435					440					445			
Phe	Ser	Leu	Ile	Ala	Val	Leu	Ile	Pro	Leu	Leu	Phe	Met	Gly	Asp	Ile
450						455					460				
Val	Gly	Arg	Leu	Phe	Arg	Glu	Phe	Ala	Ile	Thr	Leu	Ala	Val	Ala	Ile
465				470					475					480	
Leu	Ile	Ser	Ala	Val	Ser	Leu	Thr	Leu	Thr	Pro	Met	Met	Cys	Ala	
				485					490				495		
Arg	Met	Leu	Ser	Gln	Glu	Ser	Leu	Arg	Lys	Gln	Asn	Arg	Phe	Ser	Arg
			500					505					510		
Ala	Ser	Glu	Lys	Met	Phe	Asp	Arg	Ile	Ile	Ala	Ala	Tyr	Gly	Arg	Gly
		515					520					525			
Leu	Ala	Lys	Val	Leu	Asn	His	Pro	Trp	Leu	Thr	Leu	Ser	Val	Ala	Leu
530						535					540				
Ser	Thr	Leu	Leu	Leu	Ser	Val	Leu	Leu	Trp	Val	Phe	Ile	Pro	Lys	Gly
545				550					555					560	
Phe	Phe	Pro	Val	Gln	Asp	Asn	Gly	Ile	Ile	Gln	Gly	Thr	Leu	Gln	Ala
				565					570					575	
Pro	Gln	Ser	Ser	Ser	Phe	Ala	Asn	Met	Ala	Gln	Arg	Gln	Arg	Gln	Val
			580					585					590		
Ala	Asp	Val	Ile	Leu	Gln	Asp	Pro	Ala	Val	Gln	Ser	Leu	Thr	Ser	Phe
		595					600					605			
Val	Gly	Val	Asp	Gly	Thr	Asn	Pro	Ser	Leu	Asn	Ser	Ala	Arg	Leu	Gln
610						615					620				
Ile	Asn	Leu	Lys	Pro	Leu	Asp	Glu	Arg	Asp	Asp	Arg	Val	Gln	Lys	Val
625				630					635					640	
Ile	Ala	Arg	Leu	Gln	Thr	Ala	Val	Asp	Lys	Val	Pro	Gly	Val	Asp	Leu
				645					650					655	
Phe	Leu	Gln	Pro	Thr	Gln	Asp	Leu	Thr	Ile	Asp	Thr	Gln	Val	Ser	Arg
			660				665					670			
Thr	Gln	Tyr	Gln	Phe	Thr	Leu	Gln	Ala	Thr	Ser	Leu	Asp	Ala	Leu	Ser
		675					680					685			


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Thr Trp Val Pro Gln Leu Met Glu Lys Leu Gln Gln Leu Pro Gln Leu
690          695          700
Ser Asp Val Ser Ser Asp Trp Gln Asp Lys Gly Leu Val Ala Tyr Val
705          710          715          720
Asn Val Asp Arg Asp Ser Ala Ser Arg Leu Gly Ile Ser Met Ala Asp
725          730          735
Val Asp Asn Ala Leu Tyr Asn Ala Phe Gly Gln Arg Leu Ile Ser Thr
740          745          750
Ile Tyr Thr Gln Ala Asn Gln Tyr Arg Val Val Leu Glu His Asn Thr
755          760          765
Glu Asn Thr Pro Gly Leu Ala Leu Asp Thr Ile Arg Leu Thr Ser
770          775          780
Ser Asp Gly Gly Val Val Pro Leu Ser Ser Ile Ala Lys Ile Glu Gln
785          790          795          800
Arg Phe Ala Pro Leu Ser Ile Asn His Leu Asp Gln Phe Pro Val Thr
805          810          815
Thr Ile Ser Phe Asn Val Pro Asp Asn Tyr Ser Leu Gly Asp Ala Val
820          825          830
Gln Ala Ile Met Asp Thr Glu Lys Thr Leu Asn Leu Pro Val Asp Ile
835          840          845
Thr Thr Gln Phe Gln Gly Ser Thr Leu Ala Phe Gln Ser Ala Leu Gly
850          855          860
Ser Thr Val Trp Leu Ile Val Ala Ala Val Val Ala Met Tyr Ile Val
865          870          875          880
Leu Gly Ile Leu Tyr Glu Ser Phe Ile His Pro Ile Thr Ile Leu Ser
885          890          895
Thr Leu Pro Thr Ala Gly Val Gly Ala Leu Leu Ala Leu Leu Ile Ala
900          905          910
Gly Ser Glu Leu Asp Val Ile Ala Ile Ile Gly Ile Ile Leu Leu Ile
915          920          925
Gly Ile Val Lys Lys Asn Ala Ile Met Met Ile Asp Phe Ala Leu Ala
930          935          940
Ala Glu Arg Glu Gln Gly Met Ser Pro Arg Glu Ala Ile Tyr Gln Ala
945          950          955          960
Cys Leu Leu Arg Phe Arg Pro Ile Leu Met Thr Thr Leu Ala Ala Leu
965          970          975
Leu Gly Ala Leu Pro Leu Met Leu Ser Thr Gly Val Gly Ala Glu Leu
980          985          990
Arg Arg Pro Leu Gly Ile Gly Met Val Gly Gly Leu Ile Val Ser Gln
995          1000          1005
Val Leu Thr Leu Phe Thr Thr Pro Val Ile Tyr Leu Leu Phe Asp Arg
1010          1015          1020
Leu Ala Leu Trp Thr Lys Ser Arg Phe Ala Arg His Glu Glu Glu Ala
1025          1030          1035          1040

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<210> 283
 <211> 1025
 <212> PRT
 <213> E. Coli

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<400> 283
Met Lys Phe Phe Ala Leu Phe Ile Tyr Arg Pro Val Ala Thr Ile Leu
1      5      10      15
Leu Ser Val Ala Ile Thr Leu Cys Gly Ile Leu Gly Phe Arg Met Leu
20      25      30
Pro Val Ala Pro Leu Pro Gln Val Asp Phe Pro Val Ile Ile Val Ser
35      40      45
Ala Ser Leu Pro Gly Ala Ser Pro Glu Thr Met Ala Ser Ser Val Ala
50      55      60
Thr Pro Leu Glu Arg Ser Leu Gly Arg Ile Ala Gly Val Ser Glu Met

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65					70					75				80	
Thr	Ser	Ser	Ser	Ser	Leu	Gly	Ser	Thr	Arg	Ile	Ile	Leu	Gln	Phe	Asp
				85					90					95	
Phe	Asp	Arg	Asp	Ile	Asn	Gly	Ala	Ala	Arg	Asp	Val	Gln	Ala	Ala	Ile
			100					105					110		
Asn	Ala	Ala	Gln	Ser	Leu	Leu	Pro	Ser	Gly	Met	Pro	Ser	Arg	Pro	Thr
			115				120					125			
Tyr	Arg	Lys	Ala	Asn	Pro	Ser	Asp	Ala	Pro	Ile	Met	Ile	Leu	Thr	Leu
			130				135				140				
Thr	Ser	Asp	Thr	Tyr	Ser	Gln	Gly	Glu	Leu	Tyr	Asp	Phe	Ala	Ser	Thr
				150						155					160
Gln	Leu	Ala	Pro	Thr	Ile	Ser	Gln	Ile	Asp	Gly	Val	Gly	Asp	Val	Asp
				165					170					175	
Val	Gly	Gly	Ser	Ser	Leu	Pro	Ala	Val	Arg	Val	Gly	Leu	Asn	Pro	Gln
			180					185					190		
Ala	Leu	Phe	Asn	Gln	Gly	Val	Ser	Leu	Asp	Asp	Val	Arg	Thr	Ala	Val
			195				200					205			
Ser	Asn	Ala	Asn	Val	Arg	Lys	Pro	Gln	Gly	Ala	Leu	Glu	Asp	Gly	Thr
			210			215					220				
His	Arg	Trp	Gln	Ile	Gln	Thr	Asn	Asp	Glu	Leu	Lys	Thr	Ala	Ala	Glu
			225		230				235						240
Tyr	Gln	Pro	Leu	Ile	Ile	His	Tyr	Asn	Asn	Gly	Gly	Ala	Val	Arg	Leu
			245					250						255	
Gly	Asp	Val	Ala	Thr	Val	Thr	Asp	Ser	Val	Gln	Asp	Val	Arg	Asn	Ala
			260				265					270			
Gly	Met	Thr	Asn	Ala	Lys	Pro	Ala	Ile	Leu	Leu	Met	Ile	Arg	Lys	Leu
			275				280					285			
Pro	Glu	Ala	Asn	Ile	Ile	Gln	Thr	Val	Asp	Ser	Ile	Arg	Ala	Lys	Leu
			290			295					300				
Pro	Glu	Leu	Gln	Glu	Thr	Ile	Pro	Ala	Ala	Ile	Asp	Leu	Gln	Ile	Ala
			305		310					315					320
Gln	Asp	Arg	Ser	Pro	Thr	Ile	Arg	Ala	Ser	Leu	Glu	Glu	Val	Glu	Gln
			325					330						335	
Thr	Leu	Ile	Ile	Ser	Val	Ala	Leu	Val	Ile	Leu	Val	Val	Phe	Leu	Phe
			340				345						350		
Leu	Arg	Ser	Gly	Arg	Ala	Thr	Ile	Pro	Ala	Val	Ser	Val	Pro	Val	
			355				360					365			
Ser	Leu	Ile	Gly	Thr	Phe	Ala	Ala	Met	Tyr	Leu	Cys	Gly	Phe	Ser	Leu
			370			375					380				
Asn	Asn	Leu	Ser	Leu	Met	Ala	Leu	Thr	Ile	Ala	Thr	Gly	Phe	Val	Val
			385		390					395				400	
Asp	Asp	Ala	Ile	Val	Val	Leu	Glu	Asn	Ile	Ala	Arg	His	Leu	Glu	Ala
			405					410						415	
Gly	Met	Lys	Pro	Leu	Gln	Ala	Ala	Leu	Gln	Gly	Thr	Arg	Glu	Val	Gly
			420				425					430			
Phe	Thr	Val	Leu	Ser	Met	Ser	Leu	Ser	Leu	Val	Ala	Val	Phe	Leu	Pro
			435				440					445			
Leu	Leu	Leu	Met	Gly	Gly	Leu	Pro	Gly	Arg	Leu	Leu	Arg	Glu	Phe	Ala
			450			455					460				
Val	Thr	Leu	Ser	Val	Ala	Ile	Gly	Ile	Ser	Leu	Leu	Val	Ser	Leu	Thr
			465		470					475					480
Leu	Thr	Pro	Met	Met	Cys	Gly	Trp	Met	Leu	Lys	Ala	Ser	Lys	Pro	Arg
			485					490						495	
Glu	Gln	Lys	Arg	Leu	Arg	Gly	Phe	Gly	Arg	Met	Leu	Val	Ala	Leu	Gln
			500				505						510		
Gln	Gly	Tyr	Gly	Lys	Ser	Leu	Lys	Trp	Val	Leu	Asn	His	Thr	Arg	Leu
			515				520					525			
Val	Gly	Val	Val	Leu	Leu	Gly	Thr	Ile	Ala	Leu	Asn	Ile	Trp	Leu	Tyr
			530			535				540					
Ile	Ser	Ile	Pro	Lys	Thr	Phe	Phe	Pro	Glu	Gln	Asp	Thr	Gly	Val	Leu
			545		550				555					560	

Met Gly Gly Ile Gln Ala Asp Gln Ser Ile Ser Phe Gln Ala Met Arg
 565 570 575
 Gly Lys Leu Gln Asp Phe Met Lys Ile Ile Arg Asp Asp Pro Ala Val
 580 585 590
 Asp Asn Val Thr Gly Phe Thr Gly Gly Ser Arg Val Asn Ser Gly Met
 595 600 605
 Met Phe Ile Thr Leu Lys Pro Arg Asp Glu Arg Ser Glu Thr Ala Gln
 610 615 620
 Gln Ile Ile Asp Arg Leu Arg Val Lys Leu Ala Lys Glu Pro Gly Ala
 625 630 635 640
 Asn Leu Phe Leu Met Ala Val Gln Asp Ile Arg Val Gly Gly Arg Gln
 645 650 655
 Ser Asn Ala Ser Tyr Gln Tyr Thr Leu Leu Ser Asp Asp Leu Ala Ala
 660 665 670
 Leu Arg Glu Trp Glu Pro Lys Ile Arg Lys Lys Leu Ala Thr Leu Pro
 675 680 685
 Glu Leu Ala Asp Val Asn Ser Asp Gln Gln Asp Asn Gly Ala Glu Met
 690 695 700
 Asn Leu Val Tyr Asp Arg Asp Thr Met Ala Arg Leu Gly Ile Asp Val
 705 710 715 720
 Gln Ala Ala Asn Ser Leu Leu Asn Asn Ala Phe Gly Gln Arg Gln Ile
 725 730 735
 Ser Thr Ile Tyr Gln Pro Met Asn Gln Tyr Lys Val Val Met Glu Val
 740 745 750
 Asp Pro Arg Tyr Thr Gln Asp Ile Ser Ala Leu Glu Lys Met Phe Val
 755 760 765
 Ile Asn Asn Glu Gly Lys Ala Ile Pro Leu Ser Tyr Phe Ala Lys Trp
 770 775 780
 Gln Pro Ala Asn Ala Pro Leu Ser Val Asn His Gln Gly Leu Ser Ala
 785 790 795 800
 Ala Ser Thr Ile Ser Phe Asn Leu Pro Thr Gly Lys Ser Leu Ser Asp
 805 810 815
 Ala Ser Ala Ala Ile Asp Arg Ala Met Thr Gln Leu Gly Val Pro Ser
 820 825 830
 Thr Val Arg Gly Ser Phe Ala Gly Thr Ala Gln Val Phe Gln Glu Thr
 835 840 845
 Met Asn Ser Gln Val Ile Leu Ile Ile Ala Ala Ile Ala Thr Val Tyr
 850 855 860
 Ile Val Leu Gly Ile Leu Tyr Glu Ser Tyr Val His Pro Leu Thr Ile
 865 870 875 880
 Leu Ser Thr Leu Pro Ser Ala Gly Val Gly Ala Leu Leu Ala Leu Glu
 885 890 895
 Leu Phe Asn Ala Pro Phe Ser Leu Ile Ala Leu Ile Gly Ile Met Leu
 900 905 910
 Leu Ile Gly Ile Val Lys Lys Asn Ala Ile Met Met Val Asp Phe Ala
 915 920 925
 Leu Glu Ala Gln Arg His Gly Asn Leu Thr Pro Gln Glu Ala Ile Phe
 930 935 940
 Gln Ala Cys Leu Leu Arg Phe Arg Pro Ile Met Met Thr Thr Leu Ala
 945 950 955 960
 Ala Leu Phe Gly Ala Leu Pro Leu Val Leu Ser Gly Gly Asp Gly Ser
 965 970 975
 Glu Leu Arg Gln Pro Leu Gly Ile Thr Ile Val Gly Gly Leu Val Met
 980 985 990
 Ser Gln Leu Leu Thr Leu Tyr Thr Thr Pro Val Val Tyr Leu Phe Phe
 995 1000 1005
 Asp Arg Leu Arg Leu Arg Phe Ser Arg Lys Pro Lys Gln Thr Val Thr
 1010 1015 1020
 Glu
 1025

<210> 284
 <211> 471
 <212> PRT
 <213> E. Coli

<400> 284
 Met Thr Asp Leu Pro Asp Ser Thr Arg Trp Gln Leu Trp Ile Val Ala
 1 5 10 15
 Phe Gly Phe Phe Met Gln Ser Leu Asp Thr Thr Ile Val Asn Thr Ala
 20 25 30
 Leu Pro Ser Met Ala Gln Ser Leu Gly Glu Ser Pro Leu His Met His
 35 40 45
 Met Val Ile Val Ser Tyr Val Leu Thr Val Ala Val Met Leu Pro Ala
 50 55 60
 Ser Gly Trp Leu Ala Asp Lys Val Gly Val Arg Asn Ile Phe Phe Thr
 65 70 75 80
 Ala Ile Val Leu Phe Thr Leu Gly Ser Leu Phe Cys Ala Leu Ser Gly
 85 90 95
 Thr Leu Asn Glu Leu Leu Leu Ala Arg Ala Leu Gln Gly Val Gly Gly
 100 105 110
 Ala Met Met Val Pro Val Gly Arg Leu Thr Val Met Lys Ile Val Pro
 115 120 125
 Arg Glu Gln Tyr Met Ala Ala Met Thr Phe Val Thr Leu Pro Gly Gln
 130 135 140
 Val Gly Pro Leu Leu Gly Pro Ala Leu Gly Gly Leu Leu Val Glu Tyr
 145 150 155 160
 Ala Ser Trp His Trp Ile Phe Leu Ile Asn Ile Pro Val Gly Ile Ile
 165 170 175
 Gly Ala Ile Ala Thr Leu Leu Leu Met Pro Asn Tyr Thr Met Gln Thr
 180 185 190
 Arg Arg Phe Asp Leu Ser Gly Phe Leu Leu Leu Ala Val Gly Met Ala
 195 200 205
 Val Leu Thr Leu Ala Leu Asp Gly Ser Lys Gly Thr Gly Leu Ser Pro
 210 215 220
 Leu Thr Ile Ala Gly Leu Val Ala Val Gly Val Val Ala Leu Val Leu
 225 230 235 240
 Tyr Leu Leu His Ala Arg Asn Asn Asn Arg Ala Leu Phe Ser Leu Lys
 245 250 255
 Leu Phe Arg Thr Arg Thr Phe Ser Leu Gly Leu Ala Gly Ser Phe Ala
 260 265 270
 Gly Arg Ile Gly Ser Gly Met Leu Pro Phe Met Thr Pro Val Phe Leu
 275 280 285
 Gln Ile Gly Leu Gly Phe Ser Pro Phe His Ala Gly Leu Met Met Ile
 290 295 300
 Pro Met Val Leu Gly Ser Met Gly Met Lys Arg Ile Val Val Gln Val
 305 310 315 320
 Val Asn Arg Phe Gly Tyr Arg Arg Val Leu Val Ala Thr Thr Leu Gly
 325 330 335
 Leu Ser Leu Val Thr Leu Leu Phe Met Thr Thr Ala Leu Leu Gly Trp
 340 345 350
 Tyr Tyr Val Leu Pro Phe Val Leu Phe Leu Gln Gly Met Val Asn Ser
 355 360 365
 Thr Arg Phe Ser Ser Met Asn Thr Leu Thr Leu Lys Asp Leu Pro Asp
 370 375 380
 Asn Leu Ala Ser Ser Gly Asn Ser Leu Leu Ser Met Ile Met Gln Leu
 385 390 395 400
 Ser Met Ser Ile Gly Val Thr Ile Ala Gly Leu Leu Leu Gly Leu Phe
 405 410 415
 Gly Ser Gln His Val Ser Val Asp Ser Gly Thr Thr Gln Thr Val Phe
 420 425 430

Met Tyr Thr Trp Leu Ser Met Ala Leu Ile Ile Ala Leu Pro Ala Phe
 435 440 445
 Ile Phe Ala Arg Val Pro Asn Asp Thr His Gln Asn Val Ala Ile Ser
 450 455 460
 Arg Arg Lys Arg Ser Ala Gln
 465 470

<210> 285
 <211> 344
 <212> PRT
 <213> E. Coli

<400> 285
 Met Glu Ile Arg Ile Met Leu Phe Ile Leu Met Met Met Val Met Pro
 1 5 10 15
 Val Ser Tyr Ala Ala Cys Tyr Ser Glu Leu Ser Val Gln His Asn Leu
 20 25 30
 Val Val Gln Gly Asp Phe Ala Leu Thr Gln Thr Gln Met Ala Thr Tyr
 35 40 45
 Glu His Asn Phe Asn Asp Ser Ser Cys Val Ser Thr Asn Thr Ile Thr
 50 55 60
 Pro Met Ser Pro Ser Asp Ile Ile Val Gly Leu Tyr Asn Asp Thr Ile
 65 70 75 80
 Lys Leu Asn Leu His Phe Glu Trp Thr Asn Lys Asn Asn Ile Thr Leu
 85 90 95
 Ser Asn Asn Gln Thr Ser Phe Thr Ser Gly Tyr Ser Val Thr Val Thr
 100 105 110
 Pro Ala Ala Ser Asn Ala Lys Val Asn Val Ser Ala Gly Gly Gly Gly
 115 120 125
 Ser Val Met Ile Asn Gly Val Ala Thr Leu Ser Ser Ala Ser Ser Ser
 130 135 140
 Thr Arg Gly Ser Ala Ala Val Gln Phe Leu Leu Cys Leu Leu Gly Gly
 145 150 155 160
 Lys Ser Trp Asp Ala Cys Val Asn Ser Tyr Arg Asn Ala Leu Ala Gln
 165 170 175
 Asn Ala Gly Val Tyr Ser Phe Asn Leu Thr Leu Ser Tyr Asn Pro Ile
 180 185 190
 Thr Thr Thr Cys Lys Pro Asp Asp Leu Leu Ile Thr Leu Asp Ser Ile
 195 200 205
 Pro Val Ser Gln Leu Pro Ala Thr Gly Asn Lys Ala Thr Ile Asn Ser
 210 215 220
 Lys Gln Gly Asp Ile Ile Leu Arg Cys Lys Asn Leu Leu Gly Gln Gln
 225 230 235 240
 Asn Gln Thr Ser Arg Lys Met Gln Val Tyr Leu Ser Ser Ser Asp Leu
 245 250 255
 Leu Thr Asn Ser Asn Thr Ile Leu Lys Gly Ala Glu Asp Asn Gly Val
 260 265 270
 Gly Phe Ile Leu Glu Ser Asn Gly Ser Pro Val Thr Leu Leu Asn Ile
 275 280 285
 Thr Asn Ser Ser Lys Gly Tyr Thr Asn Leu Lys Glu Val Ala Ala Lys
 290 295 300
 Ser Lys Leu Thr Asp Thr Thr Val Ser Ile Pro Ile Thr Ala Ser Tyr
 305 310 315 320
 Tyr Val Tyr Asp Thr Asn Lys Val Lys Ser Gly Ala Leu Glu Ala Thr
 325 330 335
 Ala Leu Ile Asn Val Lys Tyr Asp
 340

<210> 286

<211> 826
 <212> PRT
 <213> E. Coli

<400> 286
 Met Leu Arg Met Thr Pro Leu Ala Ser Ala Ile Val Ala Leu Leu Leu
 1 5 10 15
 Gly Ile Glu Ala Tyr Ala Ala Glu Glu Thr Phe Asp Thr His Phe Met
 20 25 30
 Ile Gly Gly Met Lys Asp Gln Gln Val Ala Asn Ile Arg Leu Asp Asp
 35 40 45
 Asn Gln Pro Leu Pro Gly Gln Tyr Asp Ile Asp Ile Tyr Val Asn Lys
 50 55 60
 Gln Trp Arg Gly Lys Tyr Glu Ile Ile Val Lys Asp Asn Pro Gln Glu
 65 70 75 80
 Thr Cys Leu Ser Arg Glu Val Ile Lys Arg Leu Gly Ile Asn Ser Asp
 85 90 95
 Asn Phe Ala Ser Gly Lys Gln Cys Leu Thr Phe Glu Gln Leu Val Gln
 100 105 110
 Gly Gly Ser Tyr Thr Trp Asp Ile Gly Val Phe Arg Leu Asp Phe Ser
 115 120 125
 Val Pro Gln Ala Trp Val Glu Glu Leu Glu Ser Gly Tyr Val Pro Pro
 130 135 140
 Glu Asn Trp Glu Arg Gly Ile Asn Ala Phe Tyr Thr Ser Tyr Tyr Leu
 145 150 155 160
 Ser Gln Tyr Tyr Ser Asp Tyr Lys Ala Ser Gly Asn Asn Lys Ser Thr
 165 170 175
 Tyr Val Arg Phe Asn Ser Gly Leu Asn Leu Leu Gly Trp Gln Leu His
 180 185 190
 Ser Asp Ala Ser Phe Ser Lys Thr Asn Asn Asn Pro Gly Val Trp Lys
 195 200 205
 Ser Asn Thr Leu Tyr Leu Glu Arg Gly Phe Ala Gln Leu Leu Gly Thr
 210 215 220
 Leu Arg Val Gly Asp Met Tyr Thr Ser Ser Asp Ile Phe Asp Ser Val
 225 230 235 240
 Arg Phe Arg Gly Val Arg Leu Phe Arg Asp Met Gln Met Leu Pro Asn
 245 250 255
 Ser Lys Gln Asn Phe Thr Pro Arg Val Gln Gly Ile Ala Gln Ser Asn
 260 265 270
 Ala Leu Val Thr Ile Glu Gln Asn Gly Phe Val Val Tyr Gln Lys Glu
 275 280 285
 Val Pro Pro Gly Pro Phe Ala Ile Thr Asp Leu Gln Leu Ala Gly Gly
 290 295 300
 Gly Ala Asp Leu Asp Val Ser Val Lys Glu Ala Asp Gly Ser Val Thr
 305 310 315 320
 Thr Tyr Leu Val Pro Tyr Ala Ala Val Pro Asn Met Leu Gln Pro Gly
 325 330 335
 Val Ser Lys Tyr Asp Leu Ala Ala Gly Arg Ser His Ile Glu Gly Ala
 340 345 350
 Ser Lys Gln Ser Asp Phe Val Gln Ala Gly Tyr Gln Tyr Gly Phe Asn
 355 360 365
 Asn Leu Leu Thr Leu Tyr Gly Gly Ser Met Val Ala Asn Asn Tyr Tyr
 370 375 380
 Ala Phe Thr Leu Gly Ala Gly Trp Asn Thr Arg Ile Gly Ala Ile Ser
 385 390 395 400
 Val Asp Ala Thr Lys Ser His Ser Lys Gln Asp Asn Gly Asp Val Phe
 405 410 415
 Asp Gly Gln Ser Tyr Gln Ile Ala Tyr Asn Lys Phe Val Ser Gln Thr
 420 425 430
 Ser Thr Arg Phe Gly Leu Ala Ala Trp Arg Tyr Ser Ser Arg Asp Tyr
 435 440 445

Arg Thr Phe Asn Asp His Val Trp Ala Asn Asn Lys Asp Asn Tyr Arg
 450 455 460
 Arg Asp Glu Asn Asp Val Tyr Asp Ile Ala Asp Tyr Tyr Gln Asn Asp
 465 470 475 480
 Phe Gly Arg Lys Asn Ser Phe Ser Ala Asn Met Ser Gln Ser Leu Pro
 485 490 495
 Glu Gly Trp Gly Ser Val Ser Leu Ser Thr Leu Trp Arg Asp Tyr Trp
 500 505 510
 Gly Arg Ser Gly Ser Ser Lys Asp Tyr Gln Leu Ser Tyr Ser Asn Asn
 515 520 525
 Leu Arg Arg Ile Ser Tyr Thr Leu Ala Ala Ser Gln Ala Tyr Asp Glu
 530 535 540
 Asn His His Glu Glu Lys Arg Phe Asn Ile Phe Ile Ser Ile Pro Phe
 545 550 555 560
 Asp Trp Gly Asp Asp Val Ser Thr Pro Arg Arg Gln Ile Tyr Met Ser
 565 570 575
 Asn Ser Thr Thr Phe Asp Asp Gln Gly Phe Ala Ser Asn Asn Thr Gly
 580 585 590
 Leu Ser Gly Thr Val Gly Ser Arg Asp Gln Phe Asn Tyr Gly Val Asn
 595 600 605
 Leu Ser His Gln His Gln Gly Asn Glu Thr Thr Ala Gly Ala Asn Leu
 610 615 620
 Thr Trp Asn Ala Pro Val Ala Thr Val Asn Gly Ser Tyr Ser Gln Ser
 625 630 635 640
 Ser Thr Tyr Arg Gln Ala Gly Ala Ser Val Ser Gly Gly Ile Val Ala
 645 650 655
 Trp Ser Gly Gly Val Asn Leu Ala Asn Arg Leu Ser Glu Thr Phe Ala
 660 665 670
 Val Met Asn Ala Pro Gly Ile Lys Asp Ala Tyr Val Asn Gly Gln Lys
 675 680 685
 Tyr Arg Thr Thr Asn Arg Asn Gly Val Val Ile Tyr Asp Gly Met Thr
 690 695 700
 Pro Tyr Arg Glu Asn His Leu Met Leu Asp Val Ser Gln Ser Asp Ser
 705 710 715 720
 Glu Ala Glu Leu Arg Gly Asn Arg Lys Ile Ala Ala Pro Tyr Arg Gly
 725 730 735
 Ala Val Val Leu Val Asn Phe Asp Thr Asp Gln Arg Lys Pro Trp Phe
 740 745 750
 Ile Lys Ala Leu Arg Ala Asp Gly Gln Ser Leu Thr Phe Gly Tyr Glu
 755 760 765
 Val Asn Asp Ile His Gly His Asn Ile Gly Val Val Gly Gln Gly Ser
 770 775 780
 Gln Leu Phe Ile Arg Thr Asn Glu Val Pro Pro Ser Val Asn Val Ala
 785 790 795 800
 Ile Asp Lys Gln Gln Gly Leu Ser Cys Thr Ile Thr Phe Gly Lys Glu
 805 810 815
 Ile Asp Glu Ser Arg Asn Tyr Ile Cys Gln
 820 825

<210> 287

<211> 239

<212> PRT

<213> E. Coli

<400> 287

Met Ala Ala Ile Pro Trp Arg Pro Phe Asn Leu Arg Gly Ile Lys Met
 1 5 10 15
 Lys Gly Leu Leu Ser Leu Leu Ile Phe Ser Met Val Leu Pro Ala His
 20 25 30
 Ala Gly Ile Val Ile Tyr Gly Thr Arg Ile Ile Tyr Pro Ala Glu Asn

			35					40					45			
Lys	Glu	Val	Met	Val	Gln	Leu	Met	Asn	Gln	Gly	Asn	Arg	Ser	Ser	Leu	
	50					55					60					
Leu	Gln	Ala	Trp	Ile	Asp	Asp	Gly	Asp	Thr	Ser	Leu	Pro	Pro	Glu	Lys	
65					70					75					80	
Ile	Gln	Val	Pro	Phe	Met	Leu	Thr	Pro	Pro	Val	Ala	Lys	Ile	Gly	Ala	
				85					90					95		
Asn	Ser	Gly	Gln	Gln	Val	Lys	Ile	Lys	Ile	Met	Pro	Asn	Lys	Leu	Pro	
			100					105					110			
Thr	Asn	Lys	Glu	Ser	Ile	Phe	Tyr	Leu	Asn	Val	Leu	Asp	Ile	Pro	Pro	
	115						120					125				
Asn	Ser	Pro	Glu	Gln	Glu	Gly	Lys	Asn	Ala	Leu	Lys	Phe	Ala	Met	Gln	
	130					135					140					
Asn	Arg	Ile	Lys	Leu	Phe	Tyr	Arg	Pro	Ala	Gly	Ile	Ala	Pro	Val	Asn	
145					150					155					160	
Lys	Ala	Thr	Phe	Lys	Lys	Leu	Leu	Val	Asn	Arg	Ser	Gly	Asn	Gly	Leu	
			165						170					175		
Val	Ile	Lys	Asn	Asp	Ser	Ala	Asn	Trp	Val	Thr	Ile	Ser	Asp	Val	Lys	
			180					185					190			
Ala	Asn	Asn	Val	Lys	Val	Asn	Tyr	Glu	Thr	Ile	Met	Ile	Ala	Pro	Leu	
	195						200					205				
Glu	Ser	Gln	Ser	Val	Asn	Val	Lys	Ser	Asn	Asn	Ala	Asn	Asn	Trp	His	
	210					215					220					
Leu	Thr	Ile	Ile	Asp	Asp	His	Gly	Asn	Tyr	Ile	Ser	Asp	Lys	Ile		
225					230					235						

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<210> 288
<211> 180
<212> PRT
<213> E. Coli
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[illegible]

<210> 289

<211> 112
 <212> PRT
 <213> E. Coli

<400> 289
 Met Ser Ser Glu Arg Asp Leu Val Asn Phe Leu Gly Asp Phe Ser Met
 1 5 10 15
 Asp Val Ala Lys Ala Val Ile Ala Gly Gly Val Ala Thr Ala Ile Gly
 20 25 30
 Ser Leu Ala Ser Phe Ala Cys Val Ser Phe Gly Phe Pro Val Ile Leu
 35 40 45
 Val Gly Gly Ala Ile Leu Leu Thr Gly Ile Val Cys Thr Val Val Leu
 50 55 60
 Asn Glu Ile Asp Ala Gln Cys His Leu Ser Glu Lys Leu Lys Tyr Ala
 65 70 75 80
 Ile Arg Asp Gly Leu Lys Arg Gln Gln Glu Leu Asp Lys Trp Lys Arg
 85 90 95
 Glu Asn Met Thr Pro Phe Met Tyr Val Leu Asn Thr Pro Pro Val Ile
 100 105 110

<210> 290
 <211> 193
 <212> PRT
 <213> E. Coli

<400> 290
 Met Thr Asp Tyr Leu Leu Leu Phe Val Gly Thr Val Leu Val Asn Asn
 1 5 10 15
 Phe Val Leu Val Lys Phe Leu Gly Leu Cys Pro Phe Met Gly Val Ser
 20 25 30
 Lys Lys Leu Glu Thr Ala Met Gly Met Gly Leu Ala Thr Thr Phe Val
 35 40 45
 Met Thr Leu Ala Ser Ile Cys Ala Trp Leu Ile Asp Thr Trp Ile Leu
 50 55 60
 Ile Pro Leu Asn Leu Ile Tyr Leu Arg Thr Leu Ala Phe Ile Leu Val
 65 70 75 80
 Ile Ala Val Val Val Gln Phe Thr Glu Met Val Val Arg Lys Thr Ser
 85 90 95
 Pro Val Leu Tyr Arg Leu Leu Gly Ile Phe Leu Pro Leu Ile Thr Thr
 100 105 110
 Asn Cys Ala Val Leu Gly Val Ala Leu Leu Asn Ile Asn Leu Gly His
 115 120 125
 Asn Phe Leu Gln Ser Ala Leu Tyr Gly Phe Ser Ala Ala Val Gly Phe
 130 135 140
 Ser Leu Val Met Val Leu Phe Ala Ala Ile Arg Glu Arg Leu Ala Val
 145 150 155 160
 Ala Asp Val Pro Ala Pro Phe Arg Gly Asn Ala Ile Ala Leu Ile Thr
 165 170 175
 Ala Gly Leu Met Ser Leu Ala Phe Met Gly Phe Ser Gly Leu Val Lys
 180 185 190
 Leu

<210> 291
 <211> 192
 <212> PRT
 <213> E. Coli

<400> 291

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Met Asn Ala Ile Trp Ile Ala Val Ala Val Ser Leu Leu Gly Leu
 1           5           10           15
Ala Phe Gly Ala Ile Leu Gly Tyr Ala Ser Arg Arg Phe Ala Val Glu
 20           25           30
Asp Asp Pro Val Val Glu Lys Ile Asp Glu Ile Leu Pro Gln Ser Gln
 35           40           45
Cys Gly Gln Cys Gly Tyr Pro Gly Cys Arg Pro Tyr Ala Glu Ala Ile
 50           55           60
Ser Cys Asn Gly Glu Lys Ile Asn Arg Cys Ala Pro Gly Gly Glu Ala
 65           70           75           80
Val Met Leu Lys Ile Ala Glu Leu Leu Asn Val Glu Pro Gln Pro Leu
 85           90           95
Asp Gly Glu Ala Gln Glu Ile Thr Pro Ala Arg Met Val Ala Val Ile
 100          105          110
Asp Glu Asn Asn Cys Ile Gly Cys Thr Lys Cys Ile Gln Ala Cys Pro
 115          120          125
Val Asp Ala Ile Val Gly Ala Thr Arg Ala Met His Thr Val Met Ser
 130          135          140
Asp Leu Cys Thr Gly Cys Asn Leu Cys Val Asp Pro Cys Pro Thr His
 145          150          155          160
Cys Ile Ser Leu Gln Pro Val Ala Glu Thr Pro Asp Ser Trp Lys Trp
 165          170          175
Asp Leu Asn Thr Ile Pro Val Arg Ile Ile Pro Val Glu His His Ala
 180          185          190

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<210> 292

<211> 740

<212> PRT

<213> E. Coli

<400> 292

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Met Leu Lys Leu Phe Ser Ala Phe Arg Lys Asn Lys Ile Trp Asp Phe
 1           5           10           15
Asn Gly Gly Ile His Pro Pro Glu Met Lys Thr Gln Ser Asn Gly Thr
 20           25           30
Pro Leu Arg Gln Val Pro Leu Ala Gln Arg Phe Val Ile Pro Leu Lys
 35           40           45
Gln His Ile Gly Ala Glu Gly Glu Leu Cys Val Ser Val Gly Asp Lys
 50           55           60
Val Leu Arg Gly Gln Pro Leu Thr Arg Gly Arg Gly Lys Met Leu Pro
 65           70           75           80
Val His Ala Pro Thr Ser Gly Thr Val Thr Ala Ile Ala Pro His Ser
 85           90           95
Thr Ala His Pro Ser Ala Leu Ala Glu Leu Ser Val Ile Ile Asp Ala
 100          105          110
Asp Gly Glu Asp Cys Trp Ile Pro Arg Asp Gly Trp Ala Asp Tyr Arg
 115          120          125
Thr Arg Ser Arg Glu Glu Leu Ile Glu Arg Ile His Gln Phe Gly Val
 130          135          140
Ala Gly Leu Gly Gly Ala Gly Phe Pro Thr Gly Val Lys Leu Gln Gly
 145          150          155          160
Gly Gly Asp Lys Ile Glu Thr Leu Ile Ile Asn Ala Ala Glu Cys Glu
 165          170          175
Pro Tyr Ile Thr Ala Asp Asp Arg Leu Met Gln Asp Cys Ala Ala Gln
 180          185          190
Val Val Glu Gly Ile Arg Ile Leu Ala His Ile Leu Gln Pro Arg Glu
 195          200          205
Ile Leu Ile Gly Ile Glu Asp Asn Lys Pro Gln Ala Ile Ser Met Leu
 210          215          220

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Arg Ala Val Leu Ala Asp Ser Asn Asp Ile Ser Leu Arg Val Ile Pro
 225 230 235 240
 Thr Lys Tyr Pro Ser Gly Gly Ala Lys Gln Leu Thr Tyr Ile Leu Thr
 245 250 255
 Gly Lys Gln Val Pro His Gly Gly Arg Ser Ser Asp Ile Gly Val Leu
 260 265 270
 Met Gln Asn Val Gly Thr Ala Tyr Ala Val Lys Arg Ala Val Ile Asp
 275 280 285
 Gly Glu Pro Ile Thr Glu Arg Val Val Thr Leu Thr Gly Glu Ala Ile
 290 295 300
 Ala Arg Pro Gly Asn Val Trp Ala Arg Leu Gly Thr Pro Val Arg His
 305 310 315 320
 Leu Leu Asn Asp Ala Gly Phe Cys Pro Ser Ala Asp Gln Met Val Ile
 325 330 335
 Met Gly Gly Pro Leu Met Gly Phe Thr Leu Pro Trp Leu Asp Val Pro
 340 345 350
 Val Val Lys Ile Thr Asn Cys Leu Leu Ala Pro Ser Ala Asn Glu Leu
 355 360 365
 Gly Glu Pro Gln Glu Glu Gln Ser Cys Ile Arg Cys Ser Ala Cys Ala
 370 375 380
 Asp Ala Cys Pro Ala Asp Leu Leu Pro Gln Gln Leu Tyr Trp Phe Ser
 385 390 395 400
 Lys Gly Gln Gln His Asp Lys Ala Thr Thr His Asn Ile Ala Asp Cys
 405 410 415
 Ile Glu Cys Gly Ala Cys Ala Trp Val Cys Pro Ser Asn Ile Pro Leu
 420 425 430
 Val Gln Tyr Phe Arg Gln Glu Lys Ala Glu Ile Ala Ala Ile Arg Gln
 435 440 445
 Glu Glu Lys Arg Ala Ala Glu Ala Lys Ala Arg Phe Glu Ala Arg Gln
 450 455 460
 Ala Arg Leu Glu Arg Glu Lys Ala Ala Arg Leu Glu Arg His Lys Ser
 465 470 475 480
 Ala Ala Val Gln Pro Ala Ala Lys Asp Lys Asp Ala Ile Ala Ala Ala
 485 490 495
 Leu Ala Arg Val Lys Glu Lys Gln Ala Gln Ala Thr Gln Pro Ile Val
 500 505 510
 Ile Lys Ala Gly Glu Arg Pro Asp Asn Ser Ala Ile Ile Ala Ala Arg
 515 520 525
 Glu Ala Arg Lys Ala Gln Ala Arg Ala Lys Gln Ala Glu Leu Gln Gln
 530 535 540
 Thr Asn Asp Ala Ala Thr Val Ala Asp Pro Arg Lys Thr Ala Val Glu
 545 550 555 560
 Ala Ala Ile Ala Arg Ala Lys Ala Arg Lys Leu Glu Gln Gln Gln Ala
 565 570 575
 Asn Ala Glu Pro Glu Gln Gln Val Asp Pro Arg Lys Ala Ala Val Glu
 580 585 590
 Ala Ala Ile Ala Arg Ala Lys Ala Arg Lys Leu Glu Gln Gln Gln Ala
 595 600 605
 Asn Ala Glu Pro Glu Glu Gln Val Asp Pro Arg Lys Ala Ala Val Glu
 610 615 620
 Ala Ala Ile Ala Arg Ala Lys Ala Arg Lys Leu Glu Gln Gln Gln Ala
 625 630 635 640
 Asn Ala Glu Pro Glu Gln Gln Val Asp Pro Arg Lys Ala Ala Val Glu
 645 650 655
 Ala Ala Ile Ala Arg Ala Lys Ala Arg Lys Arg Glu Gln Gln Pro Ala
 660 665 670
 Asn Ala Glu Pro Glu Glu Gln Val Asp Pro Arg Lys Ala Ala Val Glu
 675 680 685
 Ala Ala Ile Ala Arg Ala Lys Ala Arg Lys Leu Glu Gln Gln Gln Ala
 690 695 700
 Asn Ala Val Pro Glu Glu Gln Val Asp Pro Arg Lys Ala Ala Val Ala

705		710		715		720
Ala Ala Ile Ala Arg	Ala Gln Ala Lys	Lys Ala Ala Gln Gln	Lys Val			
	725	730	735			
Val Asn Glu Asp						
	740					

<210> 293
 <211> 352
 <212> PRT
 <213> E. Coli

<400> 293

Met Val Phe Arg Ile Ala Ser Ser Pro Tyr Thr His Asn Gln Arg Gln																			
1				5				10											15
Thr Ser Arg Ile Met Leu Leu Val Leu Leu Ala Ala Val Pro Gly Ile							25												
			20																30
Ala Ala Gln Leu Trp Phe Phe Gly Trp Gly Thr Leu Val Gln Ile Leu							40												
			35																45
Leu Ala Ser Val Ser Ala Leu Leu Ala Glu Ala Leu Val Leu Lys Leu							55												
			50																60
Arg Lys Gln Ser Val Ala Ala Thr Leu Lys Asp Asn Ser Ala Leu Leu							70												
																			80
Thr Gly Leu Leu Leu Ala Val Ser Ile Pro Pro Leu Ala Pro Trp Trp																			
							85												95
Met Val Val Leu Gly Thr Val Phe Ala Val Ile Ile Ala Lys Gln Leu																			
			100																110
Tyr Gly Gly Leu Gly Gln Asn Pro Phe Asn Pro Ala Met Ile Gly Tyr							120												
			115																125
Val Val Leu Leu Ile Ser Phe Pro Val Gln Met Thr Ser Trp Leu Pro							135												
			130																140
Pro His Glu Ile Ala Val Asn Ile Pro Gly Phe Ile Asp Ala Ile Gln							150												
																			160
Val Ile Phe Ser Gly His Thr Ala Ser Gly Gly Asp Met Asn Thr Leu																			
							165												175
Arg Leu Gly Ile Asp Gly Ile Ser Gln Ala Thr Pro Leu Asp Thr Phe																			
			180																190
Lys Thr Ser Val Arg Ala Gly His Ser Val Glu Gln Ile Met Gln Tyr							200												
			195																205
Pro Ile Tyr Ser Gly Ile Leu Ala Gly Ala Gly Trp Gln Trp Val Asn							215												
																			220
Leu Ala Trp Leu Ala Gly Gly Val Trp Leu Leu Trp Gln Lys Ala Ile							230												
																			240
Arg Trp His Ile Pro Leu Ser Phe Leu Val Thr Leu Ala Leu Cys Ala																			
							245												255
Met Leu Gly Trp Leu Phe Ser Pro Glu Thr Leu Ala Ala Pro Gln Ile																			
			260																270
His Leu Leu Ser Gly Ala Thr Met Leu Gly Ala Phe Phe Ile Leu Thr							280												
			275																285
Asp Pro Val Thr Ala Ser Thr Thr Asn Arg Gly Arg Leu Ile Phe Gly							295												
																			300
Ala Leu Ala Gly Leu Leu Val Trp Leu Ile Arg Ser Phe Gly Gly Tyr							310												
																			315
Pro Asp Gly Val Ala Phe Ala Val Leu Leu Ala Asn Ile Thr Val Pro																			
							325												335
Leu Ile Asp Tyr Thr Arg Pro Arg Val Tyr Gly His Arg Lys Gly																			
			340																350
							345												

<210> 294

<211> 206
 <212> PRT
 <213> E. Coli

<400> 294
 Met Leu Lys Thr Ile Arg Lys His Gly Ile Thr Leu Ala Leu Phe Ala
 1 5 10 15
 Ala Gly Ser Thr Gly Leu Thr Ala Ala Ile Asn Gln Met Thr Lys Thr
 20 25 30
 Thr Ile Ala Glu Gln Ala Ser Leu Gln Gln Lys Ala Leu Phe Asp Gln
 35 40 45
 Val Leu Pro Ala Glu Arg Tyr Asn Asn Ala Leu Ala Gln Ser Cys Tyr
 50 55 60
 Leu Val Thr Ala Pro Glu Leu Gly Lys Gly Glu His Arg Val Tyr Ile
 65 70 75 80
 Ala Lys Gln Asp Asp Lys Pro Val Ala Ala Val Leu Glu Ala Thr Ala
 85 90 95
 Pro Asp Gly Tyr Ser Gly Ala Ile Gln Leu Leu Val Gly Ala Asp Phe
 100 105 110
 Asn Gly Thr Val Leu Gly Thr Arg Val Thr Glu His His Glu Thr Pro
 115 120 125
 Gly Leu Gly Asp Lys Ile Glu Leu Arg Leu Ser Asp Trp Ile Thr His
 130 135 140
 Phe Ala Gly Lys Lys Ile Ser Gly Ala Asp Asp Ala His Trp Ala Val
 145 150 155 160
 Lys Lys Asp Gly Gly Asp Phe Asp Gln Phe Thr Gly Ala Thr Ile Thr
 165 170 175
 Pro Arg Ala Val Val Asn Ala Val Lys Arg Ala Gly Leu Tyr Ala Gln
 180 185 190
 Thr Leu Pro Ala Gln Leu Ser Gln Leu Pro Ala Cys Gly Glu
 195 200 205

<210> 295
 <211> 231
 <212> PRT
 <213> E. Coli

<400> 295
 Met Ser Glu Ile Lys Asp Val Ile Val Gln Gly Leu Trp Lys Asn Asn
 1 5 10 15
 Ser Ala Leu Val Gln Leu Leu Gly Leu Cys Pro Leu Leu Ala Val Thr
 20 25 30
 Ser Thr Ala Thr Asn Ala Leu Gly Leu Gly Leu Ala Thr Thr Leu Val
 35 40 45
 Leu Thr Leu Thr Asn Leu Thr Ile Ser Thr Leu Arg His Trp Thr Pro
 50 55 60
 Ala Glu Ile Arg Ile Pro Ile Tyr Val Met Ile Ile Ala Ser Val Val
 65 70 75 80
 Ser Ala Val Gln Met Leu Ile Asn Ala Tyr Ala Phe Gly Leu Tyr Gln
 85 90 95
 Ser Leu Gly Ile Phe Ile Pro Leu Ile Val Thr Asn Cys Ile Val Val
 100 105 110
 Gly Arg Ala Glu Ala Phe Ala Ala Lys Lys Gly Pro Ala Leu Ser Ala
 115 120 125
 Leu Asp Gly Phe Ser Ile Gly Met Gly Ala Thr Cys Ala Met Phe Val
 130 135 140
 Leu Gly Ser Leu Arg Glu Ile Ile Gly Asn Gly Thr Leu Phe Asp Gly
 145 150 155 160
 Ala Asp Ala Leu Leu Gly Ser Trp Ala Lys Val Leu Arg Val Glu Ile
 165 170 175

Phe His Thr Asp Ser Pro Phe Leu Leu Ala Met Leu Pro Pro Gly Ala
 180 185 190
 Phe Ile Gly Leu Gly Leu Met Leu Ala Gly Lys Tyr Leu Ile Asp Glu
 195 200 205
 Arg Met Lys Lys Arg Arg Ala Glu Ala Ala Ala Glu Arg Ala Leu Pro
 210 215 220
 Asn Gly Glu Thr Gly Asn Val
 225 230

<210> 296
 <211> 211
 <212> PRT
 <213> E. Coli

<400> 296
 Met Asn Lys Ala Lys Arg Leu Glu Ile Leu Thr Arg Leu Arg Glu Asn
 1 5 10 15
 Asn Pro His Pro Thr Thr Glu Leu Asn Phe Ser Ser Pro Phe Glu Leu
 20 25 30
 Leu Ile Ala Val Leu Leu Ser Ala Gln Ala Thr Asp Val Ser Val Asn
 35 40 45
 Lys Ala Thr Ala Lys Leu Tyr Pro Val Ala Asn Thr Pro Ala Ala Met
 50 55 60
 Leu Glu Leu Gly Val Glu Gly Val Lys Thr Tyr Ile Lys Thr Ile Gly
 65 70 75 80
 Leu Tyr Asn Ser Lys Ala Glu Asn Ile Ile Lys Thr Cys Arg Ile Leu
 85 90 95
 Leu Glu Gln His Asn Gly Glu Val Pro Glu Asp Arg Ala Ala Leu Glu
 100 105 110
 Ala Leu Pro Gly Val Gly Arg Lys Thr Ala Asn Val Val Leu Asn Thr
 115 120 125
 Ala Phe Gly Trp Pro Thr Ile Ala Val Asp Thr His Ile Phe Arg Val
 130 135 140
 Cys Asn Arg Thr Gln Phe Ala Pro Gly Lys Asn Val Glu Gln Val Glu
 145 150 155 160
 Glu Lys Leu Leu Lys Val Val Pro Ala Glu Phe Lys Val Asp Cys His
 165 170 175
 His Trp Leu Ile Leu His Gly Arg Tyr Thr Cys Ile Ala Arg Lys Pro
 180 185 190
 Arg Cys Gly Ser Cys Ile Ile Glu Asp Leu Cys Glu Tyr Lys Glu Lys
 195 200 205
 Val Asp Ile
 210

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 <211> 167
 <212> PRT
 <213> E. Coli

<400> 297
 Met Lys Arg Leu His Lys Arg Phe Leu Leu Ala Thr Phe Cys Ala Leu
 1 5 10 15
 Phe Thr Ala Thr Leu Gln Ala Ala Asp Val Thr Ile Thr Val Asn Gly
 20 25 30
 Arg Val Val Ala Lys Pro Cys Thr Ile Gln Thr Lys Glu Ala Asn Val
 35 40 45
 Asn Leu Gly Asp Leu Tyr Thr Arg Asn Leu Gln Gln Pro Gly Ser Ala
 50 55 60
 Ser Gly Trp His Asn Ile Thr Leu Ser Leu Thr Asp Cys Pro Val Glu

65				70				75				80			
Thr	Ser	Ala	Val	Thr	Ala	Ile	Val	Thr	Gly	Ser	Thr	Asp	Asn	Thr	Gly
				85					90					95	
Tyr	Tyr	Lys	Asn	Glu	Gly	Thr	Ala	Glu	Asn	Ile	Gln	Ile	Glu	Leu	Arg
			100						105					110	
Asp	Asp	Gln	Asp	Ala	Ala	Leu	Lys	Asn	Gly	Asp	Ser	Lys	Thr	Val	Ile
		115					120					125			
Val	Asp	Glu	Ile	Thr	Arg	Asn	Ala	Gln	Phe	Pro	Leu	Lys	Ala	Arg	Ala
		130				135					140				
Ile	Thr	Val	Asn	Gly	Asn	Ala	Ser	Gln	Gly	Thr	Ile	Glu	Ala	Leu	Ile
145					150					155					160
Asn	Val	Ile	Tyr	Thr	Trp	Gln									
				165											

<210> 298
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 <212> PRT
 <213> E. Coli

				<400> 298											
Met	Lys	Tyr	Asn	Asn	Ile	Ile	Phe	Leu	Gly	Leu	Cys	Leu	Gly	Leu	Thr
1				5					10					15	
Thr	Tyr	Ser	Ala	Leu	Ser	Ala	Asp	Ser	Val	Ile	Lys	Ile	Ser	Gly	Arg
			20					25					30		
Val	Leu	Asp	Tyr	Gly	Cys	Thr	Val	Ser	Ser	Asp	Ser	Leu	Asn	Phe	Thr
		35				40						45			
Val	Asp	Leu	Gln	Lys	Asn	Ser	Ala	Arg	Gln	Phe	Pro	Thr	Thr	Gly	Ser
	50				55					60					
Thr	Ser	Pro	Ala	Val	Pro	Phe	Gln	Ile	Thr	Leu	Ser	Glu	Cys	Ser	Lys
65				70						75					80
Gly	Thr	Thr	Gly	Val	Arg	Val	Ala	Phe	Asn	Gly	Ile	Glu	Asp	Ala	Glu
			85					90						95	
Asn	Asn	Thr	Leu	Leu	Lys	Leu	Asp	Glu	Gly	Ser	Asn	Thr	Ala	Ser	Gly
			100					105					110		
Leu	Gly	Ile	Glu	Ile	Leu	Asp	Ala	Asn	Met	Arg	Pro	Val	Lys	Leu	Asn
		115				120					125				
Asp	Leu	His	Ala	Gly	Met	Gln	Trp	Ile	Pro	Leu	Val	Pro	Glu	Gln	Asn
	130				135						140				
Asn	Ile	Leu	Pro	Tyr	Ser	Ala	Arg	Leu	Lys	Ser	Thr	Gln	Lys	Ser	Val
145				150						155					160
Asn	Pro	Gly	Leu	Val	Arg	Ala	Ser	Ala	Thr	Phe	Thr	Leu	Glu	Phe	Gln
			165						170					175	

<210> 299
 <211> 382
 <212> PRT
 <213> E. Coli

				<400> 299											
Met	Ser	Gly	Tyr	Thr	Val	Lys	Pro	Pro	Thr	Gly	Asp	Thr	Asn	Glu	Gln
1				5					10					15	
Thr	Gln	Phe	Ile	Asp	Tyr	Phe	Asn	Leu	Phe	Tyr	Ser	Lys	Arg	Gly	Gln
			20					25					30		
Glu	Gln	Ile	Ser	Ile	Ser	Gln	Gln	Leu	Gly	Asn	Tyr	Gly	Thr	Thr	Phe
		35				40						45			
Phe	Ser	Ala	Ser	Arg	Gln	Ser	Tyr	Trp	Asn	Thr	Ser	Arg	Ser	Asp	Gln
	50					55					60				

Gln Ile Ser Phe Gly Leu Asn Val Pro Phe Gly Asp Ile Thr Thr Ser
 65 70 75 80
 Leu Asn Tyr Ser Tyr Ser Asn Asn Ile Trp Gln Asn Asp Arg Asp His
 85 90 95
 Leu Leu Ala Phe Thr Leu Asn Val Pro Phe Ser His Trp Met Arg Thr
 100 105 110
 Asp Ser Gln Ser Ala Phe Arg Asn Ser Asn Ala Ser Tyr Ser Met Ser
 115 120 125
 Asn Asp Leu Lys Gly Gly Met Thr Asn Leu Ser Gly Val Tyr Gly Thr
 130 135 140
 Leu Leu Pro Asp Asn Asn Leu Asn Tyr Ser Val Gln Val Gly Asn Thr
 145 150 155 160
 His Gly Gly Asn Thr Ser Ser Gly Thr Ser Gly Tyr Ser Ser Leu Asn
 165 170 175
 Tyr Arg Gly Ala Tyr Gly Asn Thr Asn Val Gly Tyr Ser Arg Ser Gly
 180 185 190
 Asp Ser Ser Gln Ile Tyr Tyr Gly Met Ser Gly Gly Ile Ile Ala His
 195 200 205
 Ala Asp Gly Ile Thr Phe Gly Gln Pro Leu Gly Asp Thr Met Val Leu
 210 215 220
 Val Lys Ala Pro Gly Ala Asp Asn Val Lys Ile Glu Asn Gln Thr Gly
 225 230 235 240
 Ile His Thr Asp Trp Arg Gly Tyr Ala Ile Leu Pro Phe Ala Thr Glu
 245 250 255
 Tyr Arg Glu Asn Arg Val Ala Leu Asn Ala Asn Ser Leu Ala Asp Asn
 260 265 270
 Val Glu Leu Asp Glu Thr Val Val Thr Val Ile Pro Thr His Gly Ala
 275 280 285
 Ile Ala Arg Ala Thr Phe Asn Ala Gln Ile Gly Gly Lys Val Leu Met
 290 295 300
 Thr Leu Lys Tyr Gly Asn Lys Ser Val Pro Phe Gly Ala Ile Val Thr
 305 310 315 320
 His Gly Glu Asn Lys Asn Gly Ser Ile Val Ala Glu Asn Gly Gln Val
 325 330 335
 Tyr Leu Thr Gly Leu Pro Gln Ser Gly Gln Leu Gln Val Ser Trp Gly
 340 345 350
 Lys Asp Lys Asn Ser Asn Cys Ile Val Glu Tyr Lys Leu Pro Glu Val
 355 360 365
 Ser Pro Gly Thr Leu Leu Asn Gln Gln Thr Ala Ile Cys Arg
 370 375 380

<210> 300

<211> 138

<212> PRT

<213> E. Coli

<400> 300

Met Ile Ala Ile Ala Asp Ile Leu Gln Ala Gly Glu Lys Leu Thr Ala
 1 5 10 15
 Val Ala Pro Phe Leu Ala Gly Ile Gln Asn Glu Glu Gln Tyr Thr Gln
 20 25 30
 Ala Leu Glu Leu Val Asp His Leu Leu Leu Asn Asp Pro Glu Asn Pro
 35 40 45
 Leu Leu Asp Leu Val Cys Ala Lys Ile Thr Ala Trp Glu Glu Ser Ala
 50 55 60
 Pro Glu Phe Ala Glu Phe Asn Ala Met Ala Gln Ala Met Pro Gly Gly
 65 70 75 80
 Ile Ala Val Ile Arg Thr Leu Met Asp Gln Tyr Gly Leu Thr Leu Ser
 85 90 95
 Asp Leu Pro Glu Ile Gly Ser Lys Ser Met Val Ser Arg Val Leu Ser

[illegible]

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<210> 301
<211> 104
<212> PRT
<213> E. Coli
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[illegible]

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<210> 302
<211> 2383
<212> PRT
<213> E. Coli
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			<400>	302											
Met 1	Leu	Ser	Val	Phe 5	Thr	Phe	Phe	Arg	Cys 10	Ala	Arg	Lys	Gly	Ala 15	Phe
Met	Leu	Ala	Arg 20	Ser	Gly	Lys	Val	Ser 25	Met	Ala	Thr	Lys	Lys 30	Arg	Ser
Gly	Glu	Glu 35	Ile	Asn	Asp	Arg	Gln 40	Ile	Leu	Cys	Gly	Met 45	Gly	Ile	Lys
Leu	Arg 50	Arg	Leu	Thr	Ala	Gly 55	Ile	Cys	Leu	Ile	Thr 60	Gln	Leu	Ala	Phe
Pro 65	Met	Ala	Ala	Ala 70	Ala	Gln	Gly	Val	Val 75	Asn	Ala	Ala	Thr	Gln 80	Gln
Pro	Val	Pro	Ala 85	Gln	Ile	Ala	Ile	Ala 90	Asn	Ala	Asn	Thr	Val 95	Pro	Tyr
Thr	Leu	Gly 100	Ala	Leu	Glu	Ser	Ala 105	Gln	Ser	Val	Ala	Glu	Arg 110	Phe	Gly
Ile	Ser 115	Val	Ala	Glu	Leu	Arg	Lys 120	Leu	Asn	Gln	Phe	Arg 125	Thr	Phe	Ala
Arg	Ser 130	Phe	Asp	Asn	Val	Arg	Gln 135	Gly	Asp	Glu	Leu 140	Asp	Val	Pro	Ala
Gln 145	Val	Ser	Glu	Lys 150	Lys	Leu	Thr	Pro	Pro 155	Pro	Gly	Asn	Ser	Ser	Asp
Asn	Leu	Glu	Gln 165	Gln	Ile	Ala	Ser	Thr 170	Ser	Gln	Gln	Ile	Gly 175	Ser	Leu
Leu	Ala	Glu 180	Asp	Met	Asn	Ser	Glu 185	Gln	Ala	Ala	Asn	Met 190	Ala	Arg	Gly
Trp	Ala	Ser	Ser	Gln	Ala	Ser	Gly	Ala	Met	Thr	Asp	Trp	Leu	Ser	Arg

195				200				205							
Phe	Gly	Thr	Ala	Arg	Ile	Thr	Leu	Gly	Val	Asp	Glu	Asp	Phe	Ser	Leu
210						215					220				
Lys	Asn	Ser	Gln	Phe	Asp	Phe	Leu	His	Pro	Trp	Tyr	Glu	Thr	Pro	Asp
225				230						235					240
Asn	Leu	Phe	Phe	Ser	Gln	His	Thr	Leu	His	Arg	Thr	Asp	Glu	Arg	Thr
				245						250					255
Gln	Ile	Asn	Asn	Gly	Leu	Gly	Trp	Arg	His	Phe	Thr	Pro	Thr	Trp	Met
			260					265							270
Ser	Gly	Ile	Asn	Phe	Phe	Phe	Asp	His	Asp	Leu	Ser	Arg	Tyr	His	Ser
		275					280					285			
Arg	Ala	Gly	Ile	Gly	Ala	Glu	Tyr	Trp	Arg	Asp	Tyr	Leu	Lys	Leu	Ser
	290					295					300				
Ser	Asn	Gly	Tyr	Leu	Arg	Leu	Thr	Asn	Trp	Arg	Ser	Ala	Pro	Glu	Leu
305				310						315					320
Asp	Asn	Asp	Tyr	Glu	Ala	Arg	Pro	Ala	Asn	Gly	Trp	Asp	Val	Arg	Ala
				325						330					335
Glu	Ser	Trp	Leu	Pro	Ala	Trp	Pro	His	Leu	Gly	Gly	Lys	Leu	Val	Tyr
			340					345							350
Glu	Gln	Tyr	Tyr	Gly	Asp	Glu	Val	Ala	Leu	Phe	Asp	Lys	Asp	Asp	Arg
		355				360					365				
Gln	Ser	Asn	Pro	His	Ala	Ile	Thr	Ala	Gly	Leu	Asn	Tyr	Thr	Pro	Phe
	370					375					380				
Pro	Leu	Met	Thr	Phe	Ser	Ala	Glu	Gln	Arg	Gln	Gly	Lys	Gln	Gly	Glu
385				390						395					400
Asn	Asp	Thr	Arg	Phe	Ala	Val	Asp	Phe	Thr	Trp	Gln	Pro	Gly	Ser	Ala
				405						410					415
Met	Gln	Lys	Gln	Leu	Asp	Pro	Asn	Glu	Val	Ala	Ala	Arg	Arg	Ser	Leu
			420					425							430
Ala	Gly	Ser	Arg	Tyr	Asp	Leu	Val	Asp	Arg	Asn	Asn	Asn	Ile	Val	Leu
		435						440							445
Glu	Tyr	Arg	Lys	Lys	Glu	Leu	Val	Arg	Leu	Thr	Leu	Thr	Asp	Pro	Val
	450					455					460				
Thr	Gly	Lys	Ser	Gly	Glu	Val	Lys	Ser	Leu	Val	Ser	Ser	Leu	Gln	Thr
465				470						475					480
Lys	Tyr	Ala	Leu	Lys	Gly	Tyr	Asn	Val	Glu	Ala	Thr	Ala	Leu	Glu	Ala
				485						490					495
Ala	Gly	Gly	Lys	Val	Val	Thr	Thr	Gly	Lys	Asp	Ile	Leu	Val	Thr	Leu
			500					505							510
Pro	Ala	Tyr	Arg	Phe	Thr	Ser	Thr	Pro	Glu	Thr	Asp	Asn	Thr	Trp	Pro
	515						520					525			
Ile	Glu	Val	Thr	Ala	Glu	Asp	Val	Lys	Gly	Asn	Leu	Ser	Asn	Arg	Glu
	530					535					540				
Gln	Ser	Met	Val	Val	Val	Gln	Ala	Pro	Thr	Leu	Ser	Gln	Lys	Asp	Ser
545				550						555					560
Ser	Val	Ser	Leu	Ser	Thr	Gln	Thr	Leu	Asn	Ala	Asp	Ser	His	Ser	Thr
				565						570					575
Ala	Thr	Leu	Thr	Phe	Ile	Ala	His	Asp	Ala	Ala	Gly	Asn	Pro	Val	Val
		580						585							590
Gly	Leu	Val	Leu	Ser	Thr	Arg	His	Glu	Gly	Val	Gln	Asp	Ile	Thr	Leu
	595						600					605			
Ser	Asp	Trp	Lys	Asp	Asn	Gly	Asp	Gly	Ser	Tyr	Thr	Gln	Ile	Leu	Thr
	610					615					620				
Thr	Gly	Ala	Met	Ser	Gly	Thr	Leu	Thr	Leu	Met	Pro	Gln	Leu	Asn	Gly
625				630						635					640
Val	Asp	Ala	Ala	Lys	Ala	Pro	Ala	Val	Val	Asn	Ile	Ile	Ser	Val	Ser
				645						650					655
Ser	Ser	Arg	Thr	His	Ser	Ser	Ile	Lys	Ile	Asp	Lys	Asp	Arg	Tyr	Leu
		660					665								670
Ser	Gly	Asn	Pro	Ile	Glu	Val	Thr	Val	Glu	Leu	Arg	Asp	Glu	Asn	Asp
		675					680								685

Lys Pro Val Lys Glu Gln Lys Gln Gln Leu Asn Asn Ala Val Ser Ile
 690 695 700
 Asp Asn Val Lys Pro Gly Val Thr Thr Asp Trp Lys Glu Thr Ala Asp
 705 710 715 720
 Gly Val Tyr Lys Ala Thr Tyr Thr Ala Tyr Thr Lys Gly Ser Gly Leu
 725 730 735
 Thr Ala Lys Leu Leu Met Gln Asn Trp Asn Glu Asp Leu His Thr Ala
 740 745 750
 Gly Phe Ile Ile Asp Ala Asn Pro Gln Ser Ala Lys Ile Ala Thr Leu
 755 760 765
 Ser Ala Ser Asn Asn Gly Val Leu Ala Asn Glu Asn Ala Ala Asn Thr
 770 775 780
 Val Ser Val Asn Val Ala Asp Glu Gly Ser Asn Pro Ile Asn Asp His
 785 790 795 800
 Thr Val Thr Phe Ala Val Leu Ser Gly Ser Ala Thr Ser Phe Asn Asn
 805 810 815
 Gln Asn Thr Ala Lys Thr Asp Val Asn Gly Leu Ala Thr Phe Asp Leu
 820 825 830
 Lys Ser Ser Lys Gln Glu Asp Asn Thr Val Glu Val Thr Leu Glu Asn
 835 840 845
 Gly Val Lys Gln Thr Leu Ile Val Ser Phe Val Gly Asp Ser Ser Thr
 850 855 860
 Ala Gln Val Asp Leu Gln Lys Ser Lys Asn Glu Val Val Ala Asp Gly
 865 870 875 880
 Asn Asp Ser Val Thr Met Thr Ala Thr Val Arg Asp Ala Lys Gly Asn
 885 890 895
 Leu Leu Asn Asp Val Met Val Thr Phe Asn Val Asn Ser Ala Glu Ala
 900 905 910
 Lys Leu Ser Gln Thr Glu Val Asn Ser His Asp Gly Ile Ala Thr Ala
 915 920 925
 Thr Leu Thr Ser Leu Lys Asn Gly Asp Tyr Arg Val Thr Ala Ser Val
 930 935 940
 Ser Ser Gly Ser Gln Ala Asn Gln Gln Val Asn Phe Ile Gly Asp Gln
 945 950 955 960
 Ser Thr Ala Ala Leu Thr Leu Ser Val Pro Ser Gly Asp Ile Thr Val
 965 970 975
 Thr Asn Thr Ala Pro Gln Tyr Met Thr Ala Thr Leu Gln Asp Lys Asn
 980 985 990
 Gly Asn Pro Leu Lys Asp Lys Glu Ile Thr Phe Ser Val Pro Asn Asp
 995 1000 1005
 Val Ala Ser Lys Phe Ser Ile Ser Asn Gly Gly Lys Gly Met Thr Asp
 1010 1015 1020
 Ser Asn Gly Val Ala Ile Ala Ser Leu Thr Gly Thr Leu Ala Gly Thr
 1025 1030 1035 1040
 His Met Ile Met Ala Arg Leu Ala Asn Ser Asn Val Ser Asp Ala Gln
 1045 1050 1055
 Pro Met Thr Phe Val Ala Asp Lys Asp Arg Ala Val Val Val Leu Gln
 1060 1065 1070
 Thr Ser Lys Ala Glu Ile Ile Gly Asn Gly Val Asp Glu Thr Thr Leu
 1075 1080 1085
 Thr Ala Thr Val Lys Asp Pro Ser Asn His Pro Val Ala Gly Ile Thr
 1090 1095 1100
 Val Asn Phe Thr Met Pro Gln Asp Val Ala Ala Asn Phe Thr Leu Glu
 1105 1110 1115 1120
 Asn Asn Gly Ile Ala Ile Thr Gln Ala Asn Gly Glu Ala His Val Thr
 1125 1130 1135
 Leu Lys Gly Lys Lys Ala Gly Thr His Thr Val Thr Ala Thr Leu Gly
 1140 1145 1150
 Asn Asn Asn Thr Ser Asp Ser Gln Pro Val Thr Phe Val Ala Asp Lys
 1155 1160 1165
 Ala Ser Ala Gln Val Val Leu Gln Ile Ser Lys Asp Glu Ile Thr Gly

1170	1175	1180
Asn Gly Val Asp Ser Ala Thr Leu Thr Ala Thr Val Lys Asp Gln Phe		
1185	1190	1195
Asp Asn Glu Val Asn Asn Leu Pro Val Thr Phe Ser Ser Ala Ser Ser		1200
	1205	1210
Gly Leu Thr Leu Thr Pro Gly Val Ser Asn Thr Asn Glu Ser Gly Ile		1215
	1220	1225
Ala Gln Ala Thr Leu Ala Gly Val Ala Phe Gly Glu Lys Thr Val Thr		1230
	1235	1240
Ala Ser Leu Ala Asn Asn Gly Ala Ser Asp Asn Lys Thr Val His Phe		1245
	1250	1255
Ile Gly Asp Thr Ala Ala Ala Lys Ile Ile Glu Leu Ala Pro Val Pro		1260
1265	1270	1275
Asp Ser Ile Ile Ala Gly Thr Pro Gln Asn Ser Ser Gly Ser Val Ile		1280
	1285	1290
Thr Ala Thr Val Val Asp Asn Asn Gly Phe Pro Val Lys Gly Val Thr		1295
	1300	1305
Val Asn Phe Thr Ser Asn Ala Ala Thr Ala Glu Met Thr Asn Gly Gly		1310
	1315	1320
Gln Ala Val Thr Asn Glu Gln Gly Lys Ala Thr Val Thr Tyr Thr Asn		1325
	1330	1335
Thr Arg Ser Ser Ile Glu Ser Gly Ala Arg Pro Asp Thr Val Glu Ala		1340
1345	1350	1355
Ser Leu Glu Asn Gly Ser Ser Thr Leu Ser Thr Ser Ile Asn Val Asn		1360
	1365	1370
Ala Asp Ala Ser Thr Ala His Leu Thr Leu Leu Gln Ala Leu Phe Asp		1375
	1380	1385
Thr Val Ser Ala Gly Glu Thr Thr Ser Leu Tyr Ile Glu Val Lys Asp		1390
	1395	1400
Asn Tyr Gly Asn Gly Val Pro Gln Gln Glu Val Thr Leu Ser Val Ser		1405
	1410	1415
Pro Ser Glu Gly Val Thr Pro Ser Asn Asn Ala Ile Tyr Thr Thr Asn		1420
1425	1430	1435
His Asp Gly Asn Phe Tyr Ala Ser Phe Thr Ala Thr Lys Ala Gly Val		1440
	1445	1450
Tyr Gln Leu Thr Ala Thr Leu Glu Asn Gly Asp Ser Met Gln Gln Thr		1455
	1460	1465
Val Thr Tyr Val Pro Asn Val Ala Asn Ala Glu Ile Thr Leu Ala Ala		1470
	1475	1480
Ser Lys Asp Pro Val Ile Ala Asp Asn Asn Asp Leu Thr Thr Leu Thr		1485
	1490	1495
Ala Thr Val Ala Asp Thr Glu Gly Asn Ala Ile Ala Asn Thr Glu Val		1500
1505	1510	1515
Thr Phe Thr Leu Pro Glu Asp Val Lys Ala Asn Phe Thr Leu Ser Asp		1520
	1525	1530
Gly Gly Lys Val Ile Thr Asp Ala Glu Gly Lys Ala Lys Val Thr Leu		1535
	1540	1545
Lys Gly Thr Lys Ala Gly Ala His Thr Val Thr Ala Ser Met Thr Gly		1550
	1555	1560
Gly Lys Ser Glu Gln Leu Val Val Asn Phe Ile Ala Asp Thr Leu Thr		1565
	1570	1575
Ala Gln Val Asn Leu Asn Val Thr Glu Asp Asn Phe Ile Ala Asn Asn		1580
1585	1590	1595
Val Gly Met Thr Arg Leu Gln Ala Thr Val Thr Asp Gly Asn Gly Asn		1600
	1605	1610
Pro Leu Ala Asn Glu Ala Val Thr Phe Thr Leu Pro Ala Asp Val Ser		1615
	1620	1625
Ala Ser Phe Thr Leu Gly Gln Gly Ser Ala Ile Thr Asp Ile Asn		1630
	1635	1640
Gly Lys Ala Glu Val Thr Leu Ser Gly Thr Lys Ser Gly Thr Tyr Pro		1645
	1650	1655
		1660

Val Thr Val Ser Val Asn Asn Tyr Gly Val Ser Asp Thr Lys Gln Val
 1665 1670 1675 1680
 Thr Leu Ile Ala Asp Ala Gly Thr Ala Lys Leu Ala Ser Leu Thr Ser
 1685 1690 1695
 Val Tyr Ser Phe Val Val Ser Thr Thr Glu Gly Ala Thr Met Thr Ala
 1700 1705 1710
 Ser Val Thr Asp Ala Asn Gly Asn Pro Val Glu Gly Ile Lys Val Asn
 1715 1720 1725
 Phe Arg Gly Thr Ser Val Thr Leu Ser Ser Thr Ser Val Glu Thr Asp
 1730 1735 1740
 Asp Arg Gly Phe Ala Glu Ile Leu Val Thr Ser Thr Glu Val Gly Leu
 1745 1750 1755 1760
 Lys Thr Val Ser Ala Ser Leu Ala Asp Lys Pro Thr Glu Val Ile Ser
 1765 1770 1775
 Arg Leu Leu Asn Ala Ser Ala Asp Val Asn Ser Ala Thr Ile Thr Ser
 1780 1785 1790
 Leu Glu Ile Pro Glu Gly Gln Val Met Val Ala Gln Asp Val Ala Val
 1795 1800 1805
 Lys Ala His Val Asn Asp Gln Phe Gly Asn Pro Val Ala His Gln Pro
 1810 1815 1820
 Val Thr Phe Ser Ala Glu Pro Ser Ser Gln Met Ile Ile Ser Gln Asn
 1825 1830 1835 1840
 Thr Val Ser Thr Asn Thr Gln Gly Val Ala Glu Val Thr Met Thr Pro
 1845 1850 1855
 Glu Arg Asn Gly Ser Tyr Met Val Lys Ala Ser Leu Pro Asn Gly Ala
 1860 1865 1870
 Ser Leu Glu Lys Gln Leu Glu Ala Ile Asp Glu Lys Leu Thr Leu Thr
 1875 1880 1885
 Ala Ser Ser Pro Leu Ile Gly Val Tyr Ala Pro Thr Gly Ala Thr Leu
 1890 1895 1900
 Thr Ala Thr Leu Thr Ser Ala Asn Gly Thr Pro Val Glu Gly Gln Val
 1905 1910 1915 1920
 Ile Asn Phe Ser Val Thr Pro Glu Gly Ala Thr Leu Ser Gly Gly Lys
 1925 1930 1935
 Val Arg Thr Asn Ser Ser Gly Gln Ala Pro Val Val Leu Thr Ser Asn
 1940 1945 1950
 Lys Val Gly Thr Tyr Thr Val Thr Ala Ser Phe His Asn Gly Val Thr
 1955 1960 1965
 Ile Gln Thr Gln Thr Thr Val Lys Val Thr Gly Asn Ser Ser Thr Ala
 1970 1975 1980
 His Val Ala Ser Phe Ile Ala Asp Pro Ser Thr Ile Ala Ala Thr Asn
 1985 1990 1995 2000
 Thr Asp Leu Ser Thr Leu Lys Ala Thr Val Glu Asp Gly Ser Gly Asn
 2005 2010 2015
 Leu Ile Glu Gly Leu Thr Val Tyr Phe Ala Leu Lys Ser Gly Ser Ala
 2020 2025 2030
 Thr Leu Thr Ser Leu Thr Ala Val Thr Asp Gln Asn Gly Ile Ala Thr
 2035 2040 2045
 Thr Ser Val Lys Gly Ala Met Thr Gly Ser Val Thr Val Ser Ala Val
 2050 2055 2060
 Thr Thr Ala Gly Gly Met Gln Thr Val Asp Ile Thr Leu Val Ala Gly
 2065 2070 2075 2080
 Pro Ala Asp Thr Ser Gln Ser Val Leu Lys Ser Asn Arg Ser Ser Leu
 2085 2090 2095
 Lys Gly Asp Tyr Thr Asp Ser Ala Glu Leu Arg Leu Val Leu His Asp
 2100 2105 2110
 Ile Ser Gly Asn Pro Ile Lys Val Ser Glu Gly Met Glu Phe Val Gln
 2115 2120 2125
 Ser Gly Thr Asn Val Pro Tyr Ile Lys Ile Ser Ala Ile Asp Tyr Ser
 2130 2135 2140
 Leu Asn Ile Asn Gly Asp Tyr Lys Ala Thr Val Thr Gly Gly Gly Glu

2145 2150 2155 2160
 Gly Ile Ala Thr Leu Ile Pro Val Leu Asn Gly Val His Gln Ala Gly
 2165 2170 2175
 Leu Ser Thr Thr Ile Gln Phe Thr Arg Ala Glu Asp Lys Ile Met Ser
 2180 2185 2190
 Gly Thr Val Ser Val Asn Gly Thr Asp Leu Pro Thr Thr Thr Phe Pro
 2195 2200 2205
 Ser Gln Gly Phe Thr Gly Ala Tyr Tyr Gln Leu Asn Asn Asp Asn Phe
 2210 2215 2220
 Ala Pro Gly Lys Thr Ala Ala Asp Tyr Glu Phe Ser Ser Ser Ala Ser
 2225 2230 2235 2240
 Trp Val Asp Val Asp Ala Thr Gly Lys Val Thr Phe Lys Asn Val Gly
 2245 2250 2255
 Ser Asn Ser Glu Arg Ile Thr Ala Thr Pro Lys Ser Gly Gly Pro Ser
 2260 2265 2270
 Tyr Val Tyr Glu Ile Arg Val Lys Ser Trp Trp Val Asn Ala Gly Glu
 2275 2280 2285
 Ala Phe Met Ile Tyr Ser Leu Ala Glu Asn Phe Cys Ser Ser Asn Gly
 2290 2295 2300
 Tyr Thr Leu Pro Arg Ala Asn Tyr Leu Asn His Cys Ser Ser Arg Gly
 2305 2310 2315 2320
 Ile Gly Ser Leu Tyr Ser Glu Trp Gly Asp Met Gly His Tyr Thr Thr
 2325 2330 2335
 Asp Ala Gly Phe Gln Ser Asn Met Tyr Trp Ser Ser Ser Pro Ala Asn
 2340 2345 2350
 Ser Ser Glu Gln Tyr Val Val Ser Leu Ala Thr Gly Asp Gln Ser Val
 2355 2360 2365
 Phe Glu Lys Leu Gly Phe Ala Tyr Ala Thr Cys Tyr Lys Asn Leu
 2370 2375 2380

<210> 303
 <211> 61
 <212> PRT
 <213> E. Coli

<400> 303
 Met Ser Lys Gly Ala Leu Tyr Glu Phe Asn Asn Pro Asp Gln Leu Lys
 1 5 10 15
 Ile Pro Leu Pro His Lys His Ile Ala Ser Thr Phe Asn Asp Ile Met
 20 25 30
 Ser Lys Asp Val Gly Tyr Ala Tyr Val Ser Leu Leu Tyr Ala Cys Pro
 35 40 45
 Leu Lys Thr His Ser Leu Arg Leu Asn Pro Phe Ser Lys
 50 55 60

<210> 304
 <211> 398
 <212> PRT
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<400> 304
 Met Gln Val Ala Glu Gln Arg Ile Gln Leu Ala Glu Ala Gln Ala Lys
 1 5 10 15
 Ala Val Ala Thr Gln Asp Gly Pro Gln Ile Asp Phe Ser Ala Asp Met
 20 25 30
 Glu Arg Gln Lys Met Ser Ala Glu Gly Leu Met Gly Pro Phe Ala Leu
 35 40 45
 Asn Asp Pro Ala Ala Gly Thr Thr Gly Pro Trp Tyr Thr Asn Gly Thr
 50 55 60

Phe Gly Leu Thr Ala Gly Trp His Leu Asp Ile Trp Gly Lys Asn Arg
 65 70 75 80
 Ala Glu Val Thr Ala Arg Leu Gly Thr Val Lys Ala Arg Ala Ala Glu
 85 90 95
 Arg Glu Gln Thr Arg Gln Leu Leu Ala Gly Ser Val Ala Arg Leu Tyr
 100 105 110
 Trp Glu Trp Gln Thr Gln Ala Ala Leu Asn Thr Val Leu Gln Gln Ile
 115 120 125
 Glu Lys Glu Gln Asn Thr Ile Ile Ala Thr Asp Arg Gln Leu Tyr Gln
 130 135 140
 Asn Gly Ile Thr Ser Ser Val Glu Gly Val Glu Thr Asp Ile Asn Ala
 145 150 155 160
 Ser Lys Thr Arg Gln Gln Leu Asn Asp Val Ala Gly Lys Met Lys Ile
 165 170 175
 Ile Glu Ala Arg Leu Ser Ala Leu Thr Asn Asn Gln Thr Lys Ser Leu
 180 185 190
 Lys Leu Lys Pro Val Ala Leu Pro Lys Val Ala Ser Gln Leu Pro Asp
 195 200 205
 Glu Leu Gly Tyr Ser Leu Leu Ala Arg Arg Ala Asp Leu Gln Ala Ala
 210 215 220
 His Trp Tyr Val Glu Ser Ser Leu Ser Thr Ile Asp Ala Ala Lys Ala
 225 230 235 240
 Ala Phe Tyr Pro Asp Ile Asn Leu Met Ala Phe Leu Gln Gln Asp Ala
 245 250 255
 Leu His Leu Ser Asp Leu Phe Arg His Ser Ala Gln Gln Met Gly Val
 260 265 270
 Thr Ala Gly Leu Thr Leu Pro Ile Phe Asp Ser Gly Arg Leu Asn Ala
 275 280 285
 Asn Leu Asp Ile Ala Lys Ala Glu Ser Asn Leu Ser Ile Ala Ser Tyr
 290 295 300
 Asn Lys Ala Val Val Glu Ala Val Asn Asp Val Ala Arg Ala Ala Ser
 305 310 315 320
 Gln Val Gln Thr Leu Ala Glu Lys Asn Gln His Gln Ala Gln Ile Glu
 325 330 335
 Arg Asp Ala Leu Arg Val Val Gly Leu Ala Gln Ala Arg Phe Asn Ala
 340 345 350
 Gly Ile Ile Ala Gly Ser Arg Val Ser Glu Ala Arg Ile Pro Ala Leu
 355 360 365
 Arg Glu Arg Ala Asn Gly Leu Leu Gln Gly Gln Trp Leu Asp Ala
 370 375 380
 Ser Ile Gln Leu Thr Gly Ala Leu Gly Gly Gly Tyr Lys Arg
 385 390 395

<210> 305

<211> 96

<212> PRT

<213> E. Coli

<400> 305

Met Tyr Cys His Ala Lys Leu Lys Asn Ile Ser Gln His Thr Val Ile
 1 5 10 15
 Ser Ala His Leu Phe Leu Pro Asp Tyr Ser Pro Met Asn Arg Asp Ser
 20 25 30
 Phe Tyr Pro Ala Ile Ala Cys Phe Pro Leu Leu Leu Met Leu Ala Gly
 35 40 45
 Cys Ala Pro Met His Glu Thr Arg Gln Ala Leu Ser Gln Gln Thr Pro
 50 55 60
 Ala Ala Gln Val Asp Thr Ala Leu Pro Thr Ala Leu Lys Met Val Gly
 65 70 75 80
 Gln Thr Ala Asn Gly Gly Trp Ser Ile Thr Ile Ile Asn Ser Leu Pro

85

90

95

<210> 306
 <211> 315
 <212> PRT
 <213> E. Coli

<400> 306
 Met Arg Val Leu Leu Ala Pro Met Glu Gly Val Leu Asp Ser Leu Val
 1 5 10 15
 Arg Glu Leu Leu Thr Glu Val Asn Asp Tyr Asp Leu Cys Ile Thr Glu
 20 25 30
 Phe Val Arg Val Val Asp Gln Leu Leu Pro Val Lys Val Phe His Arg
 35 40 45
 Ile Cys Pro Glu Leu Gln Asn Ala Ser Arg Thr Pro Ser Gly Thr Leu
 50 55 60
 Val Arg Val Gln Leu Leu Gly Gln Phe Pro Gln Trp Leu Ala Glu Asn
 65 70 75 80
 Ala Ala Arg Ala Val Glu Leu Gly Ser Trp Gly Val Asp Leu Asn Cys
 85 90 95
 Gly Cys Pro Ser Lys Thr Val Asn Gly Ser Gly Gly Gly Ala Thr Leu
 100 105 110
 Leu Lys Asp Pro Glu Leu Ile Tyr Gln Gly Ala Lys Ala Met Arg Glu
 115 120 125
 Ala Val Pro Ala His Leu Pro Val Ser Val Lys Val Arg Leu Gly Trp
 130 135 140
 Asp Ser Gly Glu Lys Lys Phe Glu Ile Ala Asp Ala Val Gln Gln Ala
 145 150 155 160
 Gly Ala Thr Glu Leu Val Val His Gly Arg Thr Lys Glu Gln Gly Tyr
 165 170 175
 Arg Ala Glu His Ile Asp Trp Gln Ala Ile Gly Asp Ile Arg Gln Arg
 180 185 190
 Leu Asn Ile Pro Val Ile Ala Asn Gly Glu Ile Trp Asp Trp Gln Ser
 195 200 205
 Ala Gln Gln Cys Met Ala Ile Ser Gly Cys Asp Ala Val Met Ile Gly
 210 215 220
 Arg Gly Ala Leu Asn Ile Pro Asn Leu Ser Arg Val Val Lys Tyr Asn
 225 230 235 240
 Glu Pro Arg Met Pro Trp Pro Glu Val Val Ala Leu Leu Gln Lys Tyr
 245 250 255
 Thr Arg Leu Glu Lys Gln Gly Asp Thr Gly Leu Tyr His Val Ala Arg
 260 265 270
 Ile Lys Gln Trp Leu Ser Tyr Leu Arg Lys Glu Tyr Asp Glu Ala Thr
 275 280 285
 Glu Leu Phe Gln His Val Arg Val Leu Asn Asn Ser Pro Asp Ile Ala
 290 295 300
 Arg Ala Ile Gln Ala Ile Asp Ile Glu Lys Leu
 305 310 315

<210> 307
 <211> 296
 <212> PRT
 <213> E. Coli

<400> 307
 Met Thr Ile Ser Thr Thr Ser Thr Pro His Asp Ala Val Phe Lys Ser
 1 5 10 15
 Phe Leu Arg His Pro Asp Thr Ala Arg Asp Phe Ile Asp Ile His Leu
 20 25 30

Pro Ala Pro Leu Arg Lys Leu Cys Asp Leu Thr Thr Leu Lys Leu Glu
 35 40 45
 Pro Asn Ser Phe Ile Asp Glu Asp Leu Arg Gln Tyr Tyr Ser Asp Leu
 50 55 60
 Leu Trp Ser Val Lys Thr Gln Glu Gly Val Gly Tyr Ile Tyr Val Val
 65 70 75 80
 Ile Glu His Gln Ser Lys Pro Glu Glu Leu Met Ala Phe Arg Met Met
 85 90 95
 Arg Tyr Ser Ile Ala Ala Met Gln Asn His Leu Asp Ala Gly Tyr Lys
 100 105 110
 Glu Leu Pro Leu Val Leu Pro Met Leu Phe Tyr His Gly Cys Arg Ser
 115 120 125
 Pro Tyr Pro Tyr Ser Leu Cys Trp Leu Asp Glu Phe Ala Glu Pro Ala
 130 135 140
 Ile Ala Arg Lys Ile Tyr Ser Ser Ala Phe Pro Leu Val Asp Ile Thr
 145 150 155 160
 Val Val Pro Asp Asp Glu Ile Met Gln His Arg Lys Met Ala Leu Leu
 165 170 175
 Glu Leu Ile Gln Lys His Ile Arg Gln Arg Asp Leu Leu Gly Leu Val
 180 185 190
 Asp Gln Ile Val Ser Leu Leu Val Thr Gly Asn Thr Asn Asp Arg Gln
 195 200 205
 Leu Lys Ala Leu Phe Asn Tyr Val Leu Gln Thr Gly Asp Ala Gln Arg
 210 215 220
 Phe Arg Ala Phe Ile Gly Glu Ile Ala Glu Arg Ala Pro Gln Glu Lys
 225 230 235 240
 Glu Lys Leu Met Thr Ile Ala Asp Arg Leu Arg Glu Glu Gly Ala Met
 245 250 255
 Gln Gly Lys His Glu Glu Ala Leu Arg Ile Ala Gln Glu Met Leu Asp
 260 265 270
 Arg Gly Leu Asp Arg Glu Leu Val Met Met Val Thr Arg Leu Ser Pro
 275 280 285
 Asp Asp Leu Ile Ala Gln Ser His
 290 295

<210> 308

<211> 555

<212> PRT

<213> E. Coli

<400> 308

<400> 3

Met Ala Gln Phe Val Tyr Thr Met His Arg Val Gly Lys Val Val Pro
 1 5 10 15
 Pro Lys Arg His Ile Leu Lys Asn Ile Ser Leu Ser Phe Phe Pro Gly
 20 25 30
 Ala Lys Ile Gly Val Leu Gly Leu Asn Gly Ala Gly Lys Ser Thr Leu
 35 40 45
 Leu Arg Ile Met Ala Gly Ile Asp Lys Asp Ile Glu Gly Glu Ala Arg
 50 55 60
 Pro Gln Pro Asp Ile Lys Ile Gly Tyr Leu Pro Gln Glu Pro Gln Leu
 65 70 75 80
 Asn Pro Glu His Thr Val Arg Glu Ser Ile Glu Glu Ala Val Ser Glu
 85 90 95
 Val Val Asn Ala Leu Lys Arg Leu Asp Glu Val Tyr Ala Leu Tyr Ala
 100 105 110
 Asp Pro Asp Ala Asp Phe Asp Lys Leu Ala Ala Glu Gln Gly Arg Leu
 115 120 125
 Glu Glu Ile Ile Gln Ala His Asp Gly His Asn Leu Asn Val Gln Leu
 130 135 140

Glu Arg Ala Ala Asp Ala Leu Arg Leu Pro Asp Trp Asp Ala Lys Ile
 145 150 155 160
 Ala Asn Leu Ser Gly Gly Glu Arg Arg Arg Val Ala Leu Cys Arg Leu
 165 170 175
 Leu Leu Glu Lys Pro Asp Met Leu Leu Leu Asp Glu Pro Thr Asn His
 180 185 190
 Leu Asp Ala Glu Ser Val Ala Trp Leu Glu Arg Phe Leu His Asp Phe
 195 200 205
 Glu Gly Thr Val Val Ala Ile Thr His Asp Arg Tyr Phe Leu Asp Asn
 210 215 220
 Val Ala Gly Trp Ile Leu Glu Leu Asp Arg Gly Glu Gly Ile Pro Trp
 225 230 235 240
 Glu Gly Asn Tyr Ser Ser Trp Leu Glu Gln Lys Asp Gln Arg Leu Ala
 245 250 255
 Gln Glu Ala Ser Gln Glu Ala Ala Arg Arg Lys Ser Ile Glu Lys Glu
 260 265 270
 Leu Glu Trp Val Arg Gln Gly Thr Lys Gly Arg Gln Ser Lys Gly Lys
 275 280 285
 Ala Arg Leu Ala Arg Phe Glu Glu Leu Asn Ser Thr Glu Tyr Gln Lys
 290 295 300
 Arg Asn Glu Thr Asn Glu Leu Phe Ile Pro Pro Gly Pro Arg Leu Gly
 305 310 315 320
 Asp Lys Val Leu Glu Val Ser Asn Leu Arg Lys Ser Tyr Gly Asp Arg
 325 330 335
 Leu Leu Ile Asp Asp Leu Ser Phe Ser Ile Pro Lys Gly Ala Ile Val
 340 345 350
 Gly Ile Ile Gly Pro Asn Gly Ala Gly Lys Ser Thr Leu Phe Arg Met
 355 360 365
 Ile Ser Gly Gln Glu Gln Pro Asp Ser Gly Thr Ile Thr Leu Gly Glu
 370 375 380
 Thr Val Lys Leu Ala Ser Val Asp Gln Phe Arg Asp Ser Met Asp Asn
 385 390 395 400
 Ser Lys Thr Val Trp Glu Glu Val Ser Gly Gly Leu Asp Ile Met Lys
 405 410 415
 Ile Gly Asn Thr Glu Met Pro Ser Arg Ala Tyr Val Gly Arg Phe Asn
 420 425 430
 Phe Lys Gly Val Asp Gln Gly Lys Arg Val Gly Glu Leu Ser Gly Gly
 435 440 445
 Glu Arg Gly Arg Leu His Leu Ala Lys Leu Leu Gln Val Gly Gly Asn
 450 455 460
 Met Leu Leu Leu Asp Glu Pro Thr Asn Asp Leu Asp Ile Glu Thr Leu
 465 470 475 480
 Arg Ala Leu Glu Asn Ala Leu Leu Glu Phe Pro Gly Cys Ala Met Val
 485 490 495
 Ile Ser His Asp Arg Trp Phe Leu Asp Arg Ile Ala Thr His Ile Leu
 500 505 510
 Asp Tyr Gln Asp Glu Gly Lys Val Glu Phe Phe Glu Gly Asn Phe Thr
 515 520 525
 Glu Tyr Glu Glu Tyr Lys Lys Arg Thr Leu Gly Ala Asp Ala Leu Glu
 530 535 540
 Pro Lys Arg Ile Lys Tyr Lys Arg Ile Ala Lys
 545 550

<210> 309

<211> 173

<212> PRT

<213> E. Coli

<400> 309


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Met Ser Lys Pro Lys Tyr Pro Phe Glu Lys Arg Leu Glu Val Val Asn
 1          5          10          15
His Tyr Phe Thr Thr Asp Asp Gly Tyr Arg Ile Ile Ser Ala Arg Phe
          20          25          30
Gly Val Pro Arg Thr Gln Val Arg Thr Trp Val Ala Leu Tyr Glu Lys
          35          40          45
His Gly Glu Lys Gly Leu Ile Pro Lys Pro Lys Gly Val Ser Ala Asp
 50          55          60
Pro Glu Leu Arg Ile Lys Val Val Lys Ala Val Ile Glu Gln His Met
 65          70          75          80
Ser Leu Asn Gln Ala Ala Ala His Phe Met Leu Ala Gly Ser Gly Ser
          85          90          95
Val Ala Arg Trp Leu Lys Val Tyr Glu Glu Arg Gly Glu Ala Gly Leu
          100          105          110
Arg Ala Leu Lys Ile Gly Thr Lys Arg Asn Ile Ala Ile Ser Val Asp
          115          120          125
Pro Glu Lys Ala Ala Ser Ala Leu Glu Leu Ser Lys Asp Arg Arg Ile
          130          135          140
Glu Asp Leu Glu Arg Gln Val Arg Phe Leu Glu Thr Arg Leu Met Tyr
145          150          155          160
Leu Lys Lys Leu Lys Ala Leu Ala His Pro Thr Lys Lys
          165          170

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<210> 310
 <211> 283
 <212> PRT
 <213> E. Coli

```

<400> 310
Met Lys Val Leu Asn Glu Leu Arg Gln Phe Tyr Pro Leu Asp Glu Leu
 1          5          10          15
Leu Arg Ala Ala Glu Ile Pro Arg Ser Thr Phe Tyr Tyr His Leu Lys
          20          25          30
Ala Leu Ser Lys Pro Asp Lys Tyr Ala Asp Val Lys Lys Arg Ile Ser
          35          40          45
Glu Ile Tyr His Glu Asn Arg Gly Arg Tyr Gly Tyr Arg Arg Val Thr
 50          55          60
Leu Ser Leu His Arg Glu Gly Lys Gln Ile Asn His Lys Ala Val Gln
 65          70          75          80
Arg Leu Met Gly Thr Leu Ser Leu Lys Ala Ala Ile Lys Val Lys Arg
          85          90          95
Tyr Arg Ser Tyr Arg Gly Glu Val Gly Gln Thr Ala Pro Asn Val Leu
          100          105          110
Gln Arg Asp Phe Lys Ala Thr Arg Pro Asn Glu Lys Trp Val Thr Asp
          115          120          125
Val Thr Glu Phe Ala Val Asn Gly Arg Lys Leu Tyr Leu Ser Pro Val
          130          135          140
Ile Asp Leu Phe Asn Asn Glu Val Ile Ser Tyr Ser Leu Ser Glu Arg
145          150          155          160
Pro Val Met Asn Met Val Glu Asn Met Leu Asp Gln Ala Phe Lys Lys
          165          170          175
Leu Asn Pro His Glu His Pro Val Leu His Ser Asp Gln Gly Trp Gln
          180          185          190
Tyr Arg Met Arg Arg Tyr Gln Asn Ile Leu Lys Glu His Gly Ile Lys
          195          200          205
Gln Ser Met Ser Arg Lys Gly Asn Cys Leu Asp Asn Ala Val Val Glu
          210          215          220
Cys Phe Phe Gly Thr Leu Lys Ser Glu Cys Phe Tyr Leu Asp Glu Phe
225          230          235          240
Ser Asn Ile Ser Glu Leu Lys Asp Ala Val Thr Glu Tyr Ile Glu Tyr

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Tyr Asn Ser Arg Arg Ile Ser Leu Lys Leu Lys Gly Leu Thr Pro Ile
 245 250 255
 260 265 270
 Glu Tyr Arg Asn Gln Thr Tyr Met Pro Arg Val
 275 280

<210> 311
 <211> 38
 <212> PRT
 <213> E. Coli

<400> 311
 Met Lys Val Arg Ala Ser Val Lys Lys Leu Cys Arg Asn Cys Lys Ile
 1 5 10 15
 Val Lys Arg Asp Gly Val Ile Arg Val Ile Cys Ser Ala Glu Pro Lys
 20 25 30
 His Lys Gln Arg Gln Gly
 35

<210> 312
 <211> 443
 <212> PRT
 <213> E. Coli

<400> 312
 Met Ala Lys Gln Pro Gly Leu Asp Phe Gln Ser Ala Lys Gly Gly Leu
 1 5 10 15
 Gly Glu Leu Lys Arg Arg Leu Leu Phe Val Ile Gly Ala Leu Ile Val
 20 25 30
 Phe Arg Ile Gly Ser Phe Ile Pro Ile Pro Gly Ile Asp Ala Ala Val
 35 40 45
 Leu Ala Lys Leu Leu Glu Gln Gln Arg Gly Thr Ile Ile Glu Met Phe
 50 55 60
 Asn Met Phe Ser Gly Gly Ala Leu Ser Arg Ala Ser Ile Phe Ala Leu
 65 70 75 80
 Gly Ile Met Pro Tyr Ile Ser Ala Ser Ile Ile Gln Leu Leu Thr
 85 90 95
 Val Val His Pro Thr Leu Ala Glu Ile Lys Lys Glu Gly Glu Ser Gly
 100 105 110
 Arg Arg Lys Ile Ser Gln Tyr Thr Arg Tyr Gly Thr Leu Val Leu Ala
 115 120 125
 Ile Phe Gln Ser Ile Gly Ile Ala Thr Gly Leu Pro Asn Met Pro Gly
 130 135 140
 Met Gln Gly Leu Val Ile Asn Pro Gly Phe Ala Phe Tyr Phe Thr Ala
 145 150 155 160
 Val Val Ser Leu Val Thr Gly Thr Met Phe Leu Met Trp Leu Gly Glu
 165 170 175
 Gln Ile Thr Glu Arg Gly Ile Gly Asn Gly Ile Ser Ile Ile Ile Phe
 180 185 190
 Ala Gly Ile Val Ala Gly Leu Pro Pro Ala Ile Ala His Thr Ile Glu
 195 200 205
 Gln Ala Arg Gln Gly Asp Leu His Phe Leu Val Leu Leu Leu Val Ala
 210 215 220
 Val Leu Val Phe Ala Val Thr Phe Phe Val Val Phe Val Glu Arg Gly
 225 230 235 240
 Gln Arg Arg Ile Val Val Asn Tyr Ala Lys Arg Gln Gln Gly Arg Arg
 245 250 255
 Val Tyr Ala Ala Gln Ser Thr His Leu Pro Leu Lys Val Asn Met Ala
 260 265 270
 Gly Val Ile Pro Ala Ile Phe Ala Ser Ser Ile Ile Leu Phe Pro Ala


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      275              280              285
Thr Ile Ala Ser Trp Phe Gly Gly Gly Thr Gly Trp Asn Trp Leu Thr
  290              295              300
Thr Ile Ser Leu Tyr Leu Gln Pro Gly Gln Pro Leu Tyr Val Leu Leu
  305              310              315              320
Tyr Ala Ser Ala Ile Ile Phe Phe Cys Phe Phe Tyr Thr Ala Leu Val
      325              330              335
Phe Asn Pro Arg Glu Thr Ala Asp Asn Leu Lys Lys Ser Gly Ala Phe
      340              345              350
Val Pro Gly Ile Arg Pro Gly Glu Gln Thr Ala Lys Tyr Ile Asp Lys
      355              360              365
Val Met Thr Arg Leu Thr Leu Val Gly Ala Leu Tyr Ile Thr Phe Ile
      370              375              380
Cys Leu Ile Pro Glu Phe Met Arg Asp Ala Met Lys Val Pro Phe Tyr
  385              390              395              400
Phe Gly Gly Thr Ser Leu Leu Ile Val Val Val Ile Met Asp Phe
      405              410              415
Met Ala Gln Val Gln Thr Leu Met Met Ser Ser Gln Tyr Glu Ser Ala
      420              425              430
Leu Lys Lys Ala Asn Leu Lys Gly Tyr Gly Arg
      435              440

```

<210> 313
 <211> 144
 <212> PRT
 <213> E. Coli

```

      <400> 313
Met Arg Leu Asn Thr Leu Ser Pro Ala Glu Gly Ser Lys Lys Ala Gly
  1              5              10              15
Lys Arg Leu Gly Arg Gly Ile Gly Ser Gly Leu Gly Lys Thr Gly Gly
      20              25              30
Arg Gly His Lys Gly Gln Lys Ser Arg Ser Gly Gly Gly Val Arg Arg
      35              40              45
Gly Phe Glu Gly Gly Gln Met Pro Leu Tyr Arg Arg Leu Pro Lys Phe
      50              55              60
Gly Phe Thr Ser Arg Lys Ala Ala Ile Thr Ala Glu Ile Arg Leu Ser
  65              70              75              80
Asp Leu Ala Lys Val Glu Gly Gly Val Val Asp Leu Asn Thr Leu Lys
      85              90              95
Ala Ala Asn Ile Ile Gly Ile Gln Ile Glu Phe Ala Lys Val Ile Leu
      100              105              110
Ala Gly Glu Val Thr Thr Pro Val Thr Val Arg Gly Leu Arg Val Thr
      115              120              125
Lys Gly Ala Arg Ala Ala Ile Glu Ala Ala Gly Gly Lys Ile Glu Glu
      130              135              140

```

<210> 314
 <211> 59
 <212> PRT
 <213> E. Coli

```

      <400> 314
Met Ala Lys Thr Ile Lys Ile Thr Gln Thr Arg Ser Ala Ile Gly Arg
  1              5              10              15
Leu Pro Lys His Lys Ala Thr Leu Leu Gly Leu Gly Leu Arg Arg Ile
      20              25              30
Gly His Thr Val Glu Arg Glu Asp Thr Pro Ala Ile Arg Gly Met Ile

```


35 40 45
 Asn Ala Val Ser Phe Met Val Lys Val Glu Glu
 50 55

<210> 315
 <211> 167
 <212> PRT
 <213> E. Coli

<400> 315
 Met Ala His Ile Glu Lys Gln Ala Gly Glu Leu Gln Glu Lys Leu Ile
 1 5 10 15
 Ala Val Asn Arg Val Ser Lys Thr Val Lys Gly Gly Arg Ile Phe Ser
 20 25 30
 Phe Thr Ala Leu Thr Val Val Gly Asp Gly Asn Gly Arg Val Gly Phe
 35 40 45
 Gly Tyr Gly Lys Ala Arg Glu Val Pro Ala Ala Ile Gln Lys Ala Met
 50 55 60
 Glu Lys Ala Arg Arg Asn Met Ile Asn Val Ala Leu Asn Asn Gly Thr
 65 70 75 80
 Leu Gln His Pro Val Lys Gly Val His Thr Gly Ser Arg Val Phe Met
 85 90 95
 Gln Pro Ala Ser Glu Gly Thr Gly Ile Ile Ala Gly Gly Ala Met Arg
 100 105 110
 Ala Val Leu Glu Val Ala Gly Val His Asn Val Leu Ala Lys Ala Tyr
 115 120 125
 Gly Ser Thr Asn Pro Ile Asn Val Val Arg Ala Thr Ile Asp Gly Leu
 130 135 140
 Glu Asn Met Asn Ser Pro Glu Met Val Ala Ala Lys Arg Gly Lys Ser
 145 150 155 160
 Val Glu Glu Ile Leu Gly Lys
 165

<210> 316
 <211> 117
 <212> PRT
 <213> E. Coli

<400> 316
 Met Asp Lys Lys Ser Ala Arg Ile Arg Arg Ala Thr Arg Ala Arg Arg
 1 5 10 15
 Lys Leu Gln Glu Leu Gly Ala Thr Arg Leu Val Val His Arg Thr Pro
 20 25 30
 Arg His Ile Tyr Ala Gln Val Ile Ala Pro Asn Gly Ser Glu Val Leu
 35 40 45
 Val Ala Ala Ser Thr Val Glu Lys Ala Ile Ala Glu Gln Leu Lys Tyr
 50 55 60
 Thr Gly Asn Lys Asp Ala Ala Ala Val Gly Lys Ala Val Ala Glu
 65 70 75 80
 Arg Ala Leu Glu Lys Gly Ile Lys Asp Val Ser Phe Asp Arg Ser Gly
 85 90 95
 Phe Gln Tyr His Gly Arg Val Gln Ala Leu Ala Asp Ala Ala Arg Glu
 100 105 110
 Ala Gly Leu Gln Phe
 115

<210> 317
 <211> 177

<212> PRT

<213> E. Coli

<400> 317

```

Met Ser Arg Val Ala Lys Ala Pro Val Val Val Pro Ala Gly Val Asp
 1          5          10          15
Val Lys Ile Asn Gly Gln Val Ile Thr Ile Lys Gly Lys Asn Gly Glu
      20          25          30
Leu Thr Arg Thr Leu Asn Asp Ala Val Glu Val Lys His Ala Asp Asn
      35          40          45
Thr Leu Thr Phe Gly Pro Arg Asp Gly Tyr Ala Asp Gly Trp Ala Gln
      50          55          60
Ala Gly Thr Ala Arg Ala Leu Leu Asn Ser Met Val Ile Gly Val Thr
65          70          75          80
Glu Gly Phe Thr Lys Lys Leu Gln Leu Val Gly Val Gly Tyr Arg Ala
      85          90          95
Ala Val Lys Gly Asn Val Ile Asn Leu Ser Leu Gly Phe Ser His Pro
      100          105          110
Val Asp His Gln Leu Pro Ala Gly Ile Thr Ala Glu Cys Pro Thr Gln
      115          120          125
Thr Glu Ile Val Leu Lys Gly Ala Asp Lys Gln Val Ile Gly Gln Val
      130          135          140
Ala Ala Asp Leu Arg Ala Tyr Arg Arg Pro Glu Pro Tyr Lys Gly Lys
145          150          155          160
Gly Val Arg Tyr Ala Asp Glu Val Val Arg Thr Lys Glu Ala Lys Lys
      165          170          175
Lys

```

<210> 318

<211> 130

<212> PRT

<213> E. Coli

<400> 318

```

Met Ser Met Gln Asp Pro Ile Ala Asp Met Leu Thr Arg Ile Arg Asn
 1          5          10          15
Gly Gln Ala Ala Asn Lys Ala Ala Val Thr Met Pro Ser Ser Lys Leu
      20          25          30
Lys Val Ala Ile Ala Asn Val Leu Lys Glu Glu Gly Phe Ile Glu Asp
      35          40          45
Phe Lys Val Glu Gly Asp Thr Lys Pro Glu Leu Glu Leu Thr Leu Lys
      50          55          60
Tyr Phe Gln Gly Lys Ala Val Val Glu Ser Ile Gln Arg Val Ser Arg
65          70          75          80
Pro Gly Leu Arg Ile Tyr Lys Arg Lys Asp Glu Leu Pro Lys Val Met
      85          90          95
Ala Gly Leu Gly Ile Ala Val Val Ser Thr Ser Lys Gly Val Met Thr
      100          105          110
Asp Arg Ala Ala Arg Gln Ala Gly Leu Gly Gly Glu Ile Ile Cys Tyr
      115          120          125
Val Ala
130

```

<210> 319

<211> 101

<212> PRT

<213> E. Coli

<400> 319

```

Met Ala Lys Gln Ser Met Lys Ala Arg Glu Val Lys Arg Val Ala Leu
 1          5          10          15
Ala Asp Lys Tyr Phe Ala Lys Arg Ala Glu Leu Lys Ala Ile Ile Ser
          20          25          30
Asp Val Asn Ala Ser Asp Glu Asp Arg Trp Asn Ala Val Leu Lys Leu
          35          40          45
Gln Thr Leu Pro Arg Asp Ser Ser Pro Ser Arg Gln Arg Asn Arg Cys
          50          55          60
Arg Gln Thr Gly Arg Pro His Gly Phe Leu Arg Lys Phe Gly Leu Ser
65          70          75          80
Arg Ile Lys Val Arg Glu Ala Ala Met Arg Gly Glu Ile Pro Gly Leu
          85          90          95
Lys Lys Ala Ser Trp
          100

```

<210> 320

<211> 179

<212> PRT

<213> E. Coli

<400> 320

```

Met Ala Lys Leu His Asp Tyr Tyr Lys Asp Glu Val Val Lys Lys Leu
 1          5          10          15
Met Thr Glu Phe Asn Tyr Asn Ser Val Met Gln Val Pro Arg Val Glu
          20          25          30
Lys Ile Thr Leu Asn Met Gly Val Gly Glu Ala Ile Ala Asp Lys Lys
          35          40          45
Leu Leu Asp Asn Ala Ala Ala Asp Leu Ala Ala Ile Ser Gly Gln Lys
50          55          60
Pro Leu Ile Thr Lys Ala Arg Lys Ser Val Ala Gly Phe Lys Ile Arg
65          70          75          80
Gln Gly Tyr Pro Ile Gly Cys Lys Val Thr Leu Arg Gly Glu Arg Met
          85          90          95
Trp Glu Phe Phe Glu Arg Leu Ile Thr Ile Ala Val Pro Arg Ile Arg
          100          105          110
Asp Phe Arg Gly Leu Ser Ala Lys Ser Phe Asp Gly Arg Gly Asn Tyr
          115          120          125
Ser Met Gly Val Arg Glu Gln Ile Ile Phe Pro Glu Ile Asp Tyr Asp
          130          135          140
Lys Val Asp Arg Val Arg Gly Leu Asp Ile Thr Ile Thr Thr Thr Ala
145          150          155          160
Lys Ser Asp Glu Glu Gly Arg Ala Leu Leu Ala Ala Phe Asp Phe Pro
          165          170          175
Phe Arg Lys

```

<210> 321Z

<211> 104

<212> PRT

<213> E. Coli

<400> 321

```

Met Ala Ala Lys Ile Arg Arg Asp Asp Glu Val Ile Val Leu Thr Gly
 1          5          10          15
Lys Asp Lys Gly Lys Arg Gly Lys Val Lys Asn Val Leu Ser Ser Gly
          20          25          30

```


Lys Val Ile Val Glu Gly Ile Asn Leu Val Lys Lys His Gln Lys Pro
 35 40 45
 Val Pro Ala Leu Asn Gln Pro Gly Gly Ile Val Glu Lys Glu Ala Ala
 50 55 60
 Ile Gln Val Ser Asn Val Ala Ile Phe Asn Ala Thr Gly Lys Ala
 65 70 75 80
 Asp Arg Val Gly Phe Arg Phe Glu Asp Gly Lys Lys Val Arg Phe Phe
 85 90 95
 Lys Ser Asn Ser Glu Thr Ile Lys
 100

<210> 322
 <211> 123
 <212> PRT
 <213> E. Coli

<400> 322
 Met Ile Gln Glu Gln Thr Met Leu Asn Val Ala Asp Asn Ser Gly Ala
 1 5 10 15
 Arg Arg Val Met Cys Ile Lys Val Leu Gly Gly Ser His Arg Arg Tyr
 20 25 30
 Ala Gly Val Gly Asp Ile Ile Lys Ile Thr Ile Lys Glu Ala Ile Pro
 35 40 45
 Arg Gly Lys Val Lys Lys Gly Asp Val Leu Lys Ala Val Val Val Arg
 50 55 60
 Thr Lys Lys Gly Val Arg Arg Pro Asp Gly Ser Val Ile Arg Phe Asp
 65 70 75 80
 Gly Asn Ala Cys Val Leu Leu Asn Asn Asn Ser Glu Gln Pro Ile Gly
 85 90 95
 Thr Arg Ile Phe Gly Pro Val Thr Arg Glu Leu Arg Ser Glu Lys Phe
 100 105 110
 Met Lys Ile Ile Ser Leu Ala Pro Glu Val Leu
 115 120

<210> 323
 <211> 188
 <212> PRT
 <213> E. Coli

<400> 323
 Met Phe Lys Gly Gln Lys Thr Leu Ala Ala Leu Ala Val Ser Leu Leu
 1 5 10 15
 Phe Thr Ala Pro Val Tyr Ala Ala Asp Glu Gly Ser Gly Glu Ile His
 20 25 30
 Phe Lys Gly Glu Val Ile Glu Ala Pro Cys Glu Ile His Pro Glu Asp
 35 40 45
 Ile Asp Lys Asn Ile Asp Leu Gly Gln Val Thr Thr Thr His Ile Asn
 50 55 60
 Arg Glu His His Ser Asn Lys Val Ala Val Asp Ile Arg Leu Ile Asn
 65 70 75 80
 Cys Asp Leu Pro Ala Ser Asp Asn Gly Ser Gly Met Pro Val Ser Lys
 85 90 95
 Val Gly Val Thr Phe Asp Ser Thr Ala Lys Thr Thr Gly Ala Thr Pro
 100 105 110
 Leu Leu Ser Asn Thr Ser Ala Gly Glu Ala Thr Gly Val Gly Val Arg
 115 120 125
 Leu Met Asp Lys Asn Asp Gly Asn Ile Val Leu Gly Ser Ala Ala Pro
 130 135 140
 Asp Leu Asp Leu Asp Ala Ser Ser Ser Glu Gln Thr Leu Asn Phe Phe

145 150 155 160
 Ala Trp Met Glu Gln Ile Asp Asn Ala Val Asp Val Thr Ala Gly Glu
 165 170 175
 Val Thr Ala Asn Ala Thr Tyr Val Leu Asp Tyr Lys
 180 185

<210> 324
 <211> 427
 <212> PRT
 <213> E. Coli

<400> 324
 Met Ala Asp Thr Lys Ala Lys Leu Thr Leu Asn Gly Asp Thr Ala Val
 1 5 10 15
 Glu Leu Asp Val Leu Lys Gly Thr Leu Gly Gln Asp Val Ile Asp Ile
 20 25 30
 Arg Thr Leu Gly Ser Lys Gly Val Phe Thr Phe Asp Pro Gly Phe Thr
 35 40 45
 Ser Thr Ala Ser Cys Glu Ser Lys Ile Thr Phe Ile Asp Gly Asp Glu
 50 55 60
 Gly Ile Leu Leu His Arg Gly Phe Pro Ile Asp Gln Leu Ala Thr Asp
 65 70 75 80
 Ser Asn Tyr Leu Glu Val Cys Tyr Ile Leu Leu Asn Gly Glu Lys Pro
 85 90 95
 Thr Gln Glu Gln Tyr Asp Glu Phe Lys Thr Thr Val Thr Arg His Thr
 100 105 110
 Met Ile His Glu Gln Ile Thr Arg Leu Phe His Ala Phe Arg Arg Asp
 115 120 125
 Ser His Pro Met Ala Val Met Cys Gly Ile Thr Gly Ala Leu Ala Ala
 130 135 140
 Phe Tyr His Asp Ser Leu Asp Val Asn Asn Pro Arg His Arg Glu Ile
 145 150 155 160
 Ala Ala Phe Arg Leu Leu Ser Lys Met Pro Thr Met Ala Ala Met Cys
 165 170 175
 Tyr Lys Tyr Ser Ile Gly Gln Pro Phe Val Tyr Pro Arg Asn Asp Leu
 180 185 190
 Ser Tyr Ala Gly Asn Phe Leu Asn Met Met Phe Ser Thr Pro Cys Glu
 195 200 205
 Pro Tyr Glu Val Asn Pro Ile Leu Glu Arg Ala Met Asp Arg Ile Leu
 210 215 220
 Ile Leu His Ala Asp His Glu Gln Asn Ala Ser Thr Ser Thr Val Arg
 225 230 235 240
 Thr Ala Gly Ser Ser Gly Ala Asn Pro Phe Ala Cys Ile Ala Ala Gly
 245 250 255
 Ile Ala Ser Leu Trp Gly Pro Ala His Gly Gly Ala Asn Glu Ala Ala
 260 265 270
 Leu Lys Met Leu Glu Glu Ile Ser Ser Val Lys His Ile Pro Glu Phe
 275 280 285
 Val Arg Arg Ala Lys Asp Lys Asn Asp Ser Phe Arg Leu Met Gly Phe
 290 295 300
 Gly His Arg Val Tyr Lys Asn Tyr Asp Pro Arg Ala Thr Val Met Arg
 305 310 315 320
 Glu Thr Cys His Glu Val Leu Lys Glu Leu Gly Thr Lys Asp Asp Leu
 325 330 335
 Leu Glu Val Ala Met Glu Leu Glu Asn Ile Ala Leu Asn Asp Pro Tyr
 340 345 350
 Phe Ile Glu Lys Lys Leu Tyr Pro Asn Val Asp Phe Tyr Ser Gly Ile
 355 360 365
 Ile Leu Lys Ala Met Gly Ile Pro Ser Ser Met Phe Thr Val Ile Phe
 370 375 380

Ala Met Ala Arg Thr Val Gly Trp Ile Ala His Trp Ser Glu Met His
 385 390 395 400
 Ser Asp Gly Met Lys Ile Ala Arg Pro Arg Gln Leu Tyr Thr Gly Tyr
 405 410 415
 Glu Lys Arg Asp Phe Lys Ser Asp Ile Lys Arg
 420 425

<210> 325
 <211> 477
 <212> PRT
 <213> E. Coli

<400> 325
 Met Lys Val Thr Leu Pro Glu Phe Glu Arg Ala Gly Val Met Val Val
 1 5 10 15
 Gly Asp Val Met Leu Asp Arg Tyr Trp Tyr Gly Pro Thr Ser Arg Ile
 20 25 30
 Ser Pro Glu Ala Pro Val Pro Val Lys Val Asn Thr Ile Glu Glu
 35 40 45
 Arg Pro Gly Gly Ala Ala Asn Val Ala Met Asn Ile Ala Ser Leu Gly
 50 55 60
 Ala Asn Ala Arg Leu Val Gly Leu Thr Gly Ile Asp Asp Ala Ala Arg
 65 70 75 80
 Ala Leu Ser Lys Ser Leu Ala Asp Val Asn Val Lys Cys Asp Phe Val
 85 90 95
 Ser Val Pro Thr His Pro Thr Ile Thr Lys Leu Arg Val Leu Ser Arg
 100 105 110
 Asn Gln Gln Leu Ile Arg Leu Asp Phe Glu Glu Gly Phe Glu Gly Val
 115 120 125
 Asp Pro Gln Pro Leu His Glu Arg Ile Asn Gln Ala Leu Ser Ser Ile
 130 135 140
 Gly Ala Leu Val Leu Ser Asp Tyr Ala Lys Gly Ala Leu Ala Ser Val
 145 150 155 160
 Gln Gln Met Ile Gln Leu Ala Arg Lys Ala Gly Val Pro Val Leu Ile
 165 170 175
 Asp Pro Lys Gly Thr Asp Phe Glu Arg Tyr Arg Gly Ala Thr Leu Leu
 180 185 190
 Thr Pro Asn Leu Ser Glu Phe Glu Ala Val Val Gly Lys Cys Lys Thr
 195 200 205
 Glu Glu Glu Ile Val Glu Arg Gly Met Lys Leu Ile Ala Asp Tyr Glu
 210 215 220
 Leu Ser Ala Leu Leu Val Thr Arg Ser Glu Gln Gly Met Ser Leu Leu
 225 230 235 240
 Gln Pro Gly Lys Ala Pro Leu His Met Pro Thr Gln Ala Gln Glu Val
 245 250 255
 Tyr Asp Val Thr Gly Ala Gly Asp Thr Val Ile Gly Val Leu Ala Ala
 260 265 270
 Thr Leu Ala Ala Gly Asn Ser Leu Glu Glu Ala Cys Phe Phe Ala Asn
 275 280 285
 Ala Ala Ala Gly Val Val Val Gly Lys Leu Gly Thr Ser Thr Val Ser
 290 295 300
 Pro Ile Glu Leu Glu Asn Ala Val Arg Gly Arg Ala Asp Thr Gly Phe
 305 310 315 320
 Gly Val Met Thr Glu Glu Glu Leu Lys Leu Ala Val Ala Ala Ala Arg
 325 330 335
 Lys Arg Gly Glu Lys Val Val Met Thr Asn Gly Val Phe Asp Ile Leu
 340 345 350
 His Ala Gly His Val Ser Tyr Leu Ala Asn Ala Arg Lys Leu Gly Asp
 355 360 365
 Arg Leu Ile Val Ala Val Asn Ser Asp Ala Ser Thr Lys Arg Leu Lys

370
 Gly Asp Ser Arg Pro Val Asn Pro Leu Glu Gln Arg Met Ile Val Leu
 385
 Gly Ala Leu Glu Ala Val Asp Trp Val Val Ser Phe Glu Glu Asp Thr
 405
 Pro Gln Arg Leu Ile Ala Gly Ile Leu Pro Asp Leu Leu Val Lys Gly
 420
 Gly Asp Tyr Lys Pro Glu Glu Ile Ala Gly Ser Lys Glu Val Trp Ala
 435
 Asn Gly Glu Glu Val Leu Val Leu Asn Phe Glu Asp Gly Cys Ser Thr
 450
 Thr Asn Ile Ile Lys Lys Ile Gln Gln Asp Lys Lys Gly
 465
 470
 475

<210> 326
 <211> 946
 <212> PRT
 <213> E. Coli

<400> 326
 Met Lys Pro Leu Ser Ser Pro Leu Gln Gln Tyr Trp Gln Thr Val Val
 1
 Glu Arg Leu Pro Glu Pro Leu Ala Glu Glu Ser Leu Ser Ala Gln Ala
 20
 Lys Ser Val Leu Thr Phe Ser Asp Phe Val Gln Asp Ser Val Ile Ala
 35
 His Pro Glu Trp Leu Thr Glu Leu Glu Ser Gln Pro Pro Gln Ala Asp
 50
 Glu Trp Gln His Tyr Ala Ala Trp Leu Gln Glu Ala Leu Cys Asn Val
 65
 Ser Asp Glu Ala Gly Leu Met Arg Glu Leu Arg Leu Phe Arg Arg Arg
 85
 Ile Met Val Arg Ile Ala Trp Ala Gln Thr Leu Ala Leu Val Thr Glu
 100
 Glu Ser Ile Leu Gln Gln Leu Ser Tyr Leu Ala Glu Thr Leu Ile Val
 115
 Ala Ala Arg Asp Trp Leu Tyr Asp Ala Cys Cys Arg Glu Trp Gly Thr
 130
 Pro Cys Asn Ala Gln Gly Glu Ala Gln Pro Leu Leu Ile Leu Gly Met
 145
 Gly Lys Leu Gly Gly Gly Glu Leu Asn Phe Ser Ser Asp Ile Asp Leu
 165
 Ile Phe Ala Trp Pro Glu His Gly Cys Thr Gln Gly Gly Arg Arg Glu
 180
 Leu Asp Asn Ala Gln Phe Phe Thr Arg Met Gly Gln Arg Leu Ile Lys
 195
 Val Leu Asp Gln Pro Thr Gln Asp Gly Phe Val Tyr Arg Val Asp Met
 210
 Arg Leu Arg Pro Phe Gly Glu Ser Gly Pro Leu Val Leu Ser Phe Ala
 225
 Ala Leu Glu Asp Tyr Tyr Gln Glu Gln Gly Arg Asp Trp Glu Arg Tyr
 245
 Ala Met Val Lys Ala Arg Ile Met Gly Asp Ser Glu Gly Val Tyr Ala
 260
 Asn Glu Leu Arg Ala Met Leu Arg Pro Phe Val Phe Arg Arg Tyr Ile
 275
 Asp Phe Ser Val Ile Gln Ser Leu Arg Asn Met Lys Gly Met Ile Ala
 290
 Arg Glu Val Arg Arg Arg Gly Leu Thr Asp Asn Ile Lys Leu Gly Ala
 305
 310
 315
 320

Gly Gly Ile Arg Glu Ile Glu Phe Ile Val Gln Val Phe Gln Leu Ile
 325 330 335
 Arg Gly Gly Arg Glu Pro Ser Leu Gln Ser Arg Ser Leu Leu Pro Thr
 340 345 350
 Leu Ser Ala Ile Ala Glu Leu His Leu Leu Ser Glu Asn Asp Ala Glu
 355 360 365
 Gln Leu Arg Val Ala Tyr Leu Phe Leu Arg Arg Leu Glu Asn Leu Leu
 370 375 380
 Gln Ser Ile Asn Asp Glu Gln Thr Gln Thr Leu Pro Ser Asp Glu Leu
 385 390 395 400
 Asn Arg Ala Arg Leu Ala Trp Ala Met Asp Phe Ala Asp Trp Pro Gln
 405 410 415
 Leu Thr Gly Ala Leu Thr Ala His Met Thr Asn Val Arg Arg Val Phe
 420 425 430
 Asn Glu Leu Ile Gly Asp Asp Glu Ser Glu Thr Gln Glu Glu Ser Leu
 435 440 445
 Ser Glu Gln Trp Arg Glu Leu Trp Gln Asp Ala Leu Gln Glu Asp Asp
 450 455 460
 Thr Thr Pro Val Leu Ala His Leu Ser Glu Asp Asp Arg Lys Gln Val
 465 470 475 480
 Leu Thr Leu Ile Ala Asp Phe Arg Lys Glu Leu Asp Lys Arg Thr Ile
 485 490 495
 Gly Pro Arg Gly Arg Gln Val Leu Asp His Leu Met Pro His Leu Leu
 500 505 510
 Ser Asp Val Cys Ala Arg Glu Asp Ala Ala Val Thr Leu Ser Arg Ile
 515 520 525
 Thr Ala Leu Leu Val Gly Ile Val Thr Arg Thr Thr Tyr Leu Glu Leu
 530 535 540
 Leu Ser Glu Phe Pro Ala Ala Leu Lys His Leu Ile Ser Leu Cys Ala
 545 550 555 560
 Ala Ser Pro Met Ile Ala Ser Gln Leu Ala Arg Tyr Pro Leu Leu Leu
 565 570 575
 Asp Glu Leu Leu Asp Pro Asn Thr Leu Tyr Gln Pro Thr Ala Thr Asp
 580 585 590
 Ala Tyr Arg Asp Glu Leu Arg Gln Tyr Leu Leu Arg Val Pro Glu Asp
 595 600 605
 Asp Glu Glu Gln Gln Leu Glu Ala Leu Arg Gln Phe Lys Gln Ala Gln
 610 615 620
 Leu Leu Arg Ile Ala Ala Ala Asp Ile Ala Gly Thr Leu Pro Val Met
 625 630 635 640
 Lys Val Ser Asp His Leu Thr Trp Leu Ala Glu Ala Met Ile Asp Ala
 645 650 655
 Val Val Gln Gln Ala Trp Val Gln Met Val Ala Arg Tyr Gly Lys Pro
 660 665 670
 Asn His Leu Asn Glu Arg Glu Gly Arg Gly Phe Ala Val Val Gly Tyr
 675 680 685
 Gly Lys Leu Gly Gly Trp Glu Leu Gly Tyr Ser Ser Asp Leu Asp Leu
 690 695 700
 Ile Phe Leu His Asp Cys Pro Met Asp Ala Met Thr Asp Gly Glu Arg
 705 710 715 720
 Glu Ile Asp Gly Arg Gln Phe Tyr Leu Arg Leu Ala Gln Arg Ile Met
 725 730 735
 His Leu Phe Ser Thr Arg Thr Ser Ser Gly Ile Leu Tyr Glu Val Asp
 740 745 750
 Ala Arg Leu Arg Pro Ser Gly Ala Ala Gly Met Leu Val Thr Ser Ala
 755 760 765
 Glu Ala Phe Ala Asp Tyr Gln Lys Asn Glu Ala Trp Thr Trp Glu His
 770 775 780
 Gln Ala Leu Val Arg Ala Arg Val Val Tyr Gly Asp Pro Gln Leu Thr
 785 790 795 800
 Ala His Phe Asp Ala Val Arg Arg Glu Ile Met Thr Leu Pro Arg Glu

805								810				815			
Gly	Lys	Thr	Leu	Gln	Thr	Glu	Val	Arg	Glu	Met	Arg	Glu	Lys	Met	Arg
820								825				830			
Ala	His	Leu	Gly	Asn	Lys	His	Arg	Asp	Arg	Phe	Asp	Ile	Lys	Ala	Asp
835								840				845			
Glu	Gly	Gly	Ile	Thr	Asp	Ile	Glu	Phe	Ile	Thr	Gln	Tyr	Leu	Val	Leu
850								855				860			
Arg	Tyr	Ala	His	Glu	Lys	Pro	Lys	Leu	Thr	Arg	Trp	Ser	Asp	Asn	Val
865								870				875			
Arg	Ile	Leu	Glu	Leu	Leu	Ala	Gln	Asn	Asp	Ile	Met	Glu	Glu	Gln	Glu
885								890				895			
Ala	Met	Ala	Leu	Thr	Arg	Ala	Tyr	Thr	Thr	Leu	Arg	Asp	Glu	Leu	His
900								905				910			
His	Leu	Ala	Leu	Gln	Glu	Leu	Pro	Gly	His	Val	Ser	Glu	Asp	Cys	Phe
915								920				925			
Thr	Ala	Glu	Arg	Glu	Leu	Val	Arg	Ala	Ser	Trp	Gln	Lys	Trp	Leu	Val
930								935				940			
Glu	Glu														
945															

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<210> 327
<211> 433
<212> PRT
<213> E. Coli
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				<400>	327											
Met	Ala	Gln	Glu	Ile	Glu	Leu	Lys	Phe	Ile	Val	Asn	His	Ser	Ala	Val	
1				5					10					15		
Glu	Ala	Leu	Arg	Asp	His	Leu	Asn	Thr	Leu	Gly	Gly	Glu	His	His	Asp	
			20					25					30			
Pro	Val	Gln	Leu	Leu	Asn	Ile	Tyr	Tyr	Glu	Thr	Pro	Asp	Asn	Trp	Leu	
		35					40					45				
Arg	Gly	His	Asp	Met	Gly	Leu	Arg	Ile	Arg	Gly	Glu	Asn	Gly	Arg	Tyr	
	50					55					60					
Glu	Met	Thr	Met	Lys	Val	Ala	Gly	Arg	Val	Thr	Gly	Gly	Leu	His	Gln	
65				70					75					80		
Arg	Pro	Glu	Tyr	Asn	Val	Ala	Leu	Ser	Glu	Pro	Thr	Leu	Asp	Leu	Ala	
				85					90					95		
Gln	Leu	Pro	Thr	Glu	Val	Trp	Pro	Asn	Gly	Glu	Leu	Pro	Ala	Asp	Leu	
			100					105					110			
Ala	Ser	Arg	Val	Gln	Pro	Leu	Phe	Ser	Thr	Asp	Phe	Tyr	Arg	Glu	Lys	
	115						120					125				
Trp	Leu	Val	Ala	Val	Asp	Gly	Ser	Gln	Ile	Glu	Ile	Ala	Leu	Asp	Gln	
	130					135					140					
Gly	Glu	Val	Lys	Ala	Gly	Glu	Phe	Ala	Glu	Pro	Ile	Cys	Glu	Leu	Glu	
145				150					155					160		
Leu	Glu	Leu	Leu	Ser	Gly	Asp	Thr	Arg	Ala	Val	Leu	Lys	Leu	Ala	Asn	
				165					170					175		
Gln	Leu	Val	Ser	Gln	Thr	Gly	Leu	Arg	Gln	Gly	Ser	Leu	Ser	Lys	Ala	
			180					185				190				
Ala	Arg	Gly	Tyr	His	Leu	Ala	Gln	Gly	Asn	Pro	Ala	Arg	Glu	Ile	Lys	
	195						200					205				
Pro	Thr	Thr	Ile	Leu	His	Val	Ala	Ala	Lys	Ala	Asp	Val	Glu	Gln	Gly	
	210					215					220					
Leu	Glu	Ala	Ala	Leu	Glu	Leu	Ala	Leu	Ala	Gln	Trp	Gln	Tyr	His	Glu	
225				230					235					240		
Glu	Leu	Trp	Val	Arg	Gly	Asn	Asp	Ala	Ala	Lys	Glu	Gln	Val	Leu	Ala	
				245					250					255		
Ala	Ile	Ser	Leu	Val	Arg	His	Thr	Leu	Met	Leu	Phe	Gly	Gly	Ile	Val	


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      260      265      270
Pro Arg Lys Ala Ser Thr His Leu Arg Asp Leu Leu Thr Gln Cys Glu
      275      280      285
Ala Thr Ile Ala Ser Ala Val Ser Ala Val Thr Ala Val Tyr Ser Thr
      290      295      300
Glu Thr Ala Met Ala Lys Leu Ala Leu Thr Glu Trp Leu Val Ser Lys
305      310      315      320
Ala Trp Gln Pro Phe Leu Asp Ala Lys Ala Gln Gly Lys Ile Ser Asp
      325      330      335
Ser Phe Lys Arg Phe Ala Asp Ile His Leu Ser Arg His Ala Ala Glu
      340      345      350
Leu Lys Ser Val Phe Cys Gln Pro Leu Gly Asp Arg Tyr Arg Asp Gln
      355      360      365
Leu Pro Arg Leu Thr Arg Asp Ile Asp Ser Ile Leu Leu Leu Ala Gly
      370      375      380
Tyr Tyr Asp Pro Val Val Ala Gln Ala Trp Leu Glu Asn Trp Gln Gly
385      390      395      400
Leu His His Ala Ile Ala Thr Gly Gln Arg Ile Glu Ile Glu His Phe
      405      410      415
Arg Asn Glu Ala Asn Asn Gln Glu Pro Phe Trp Leu His Ser Gly Lys
      420      425      430
Arg

```

<210> 328
 <211> 70
 <212> PRT
 <213> E. Coli

```

      <400> 328
Met Ser Gly Lys Met Thr Gly Ile Val Lys Trp Phe Asn Ala Asp Lys
 1      5      10      15
Gly Phe Gly Phe Ile Thr Pro Asp Asp Gly Ser Lys Asp Val Phe Val
      20      25      30
His Phe Ser Ala Ile Gln Asn Asp Gly Tyr Lys Ser Leu Asp Glu Gly
      35      40      45
Gln Lys Val Ser Phe Thr Ile Glu Ser Gly Ala Lys Gly Pro Ala Ala
      50      55      60
Gly Asn Val Thr Ser Leu
65      70

```

<210> 329
 <211> 523
 <212> PRT
 <213> E. Coli

```

      <400> 329
Met Arg Asp Ile Val Asp Pro Val Phe Ser Ile Gly Ile Ser Ser Leu
 1      5      10      15
Trp Asp Glu Leu Arg His Met Pro Ala Gly Gly Val Trp Trp Phe Asn
      20      25      30
Val Asp Arg His Glu Asp Ala Ile Ser Leu Ala Asn Gln Thr Ile Ala
      35      40      45
Ser Gln Ala Glu Thr Ala His Val Ala Val Ile Ser Met Asp Ser Asp
      50      55      60
Pro Ala Lys Ile Phe Gln Leu Asp Asp Ser Gln Gly Pro Glu Lys Ile
65      70      75      80

```


Lys Leu Phe Ser Met Leu Asn His Glu Lys Gly Leu Tyr Tyr Leu Thr
 85 90 95
 Arg Asp Leu Gln Cys Ser Ile Asp Pro His Asn Tyr Leu Phe Ile Leu
 100 105 110
 Val Cys Ala Asn Asn Ala Trp Gln Asn Ile Pro Ala Glu Arg Leu Arg
 115 120 125
 Ser Trp Leu Asp Lys Met Asn Lys Trp Ser Arg Leu Asn His Cys Ser
 130 135 140
 Leu Leu Val Ile Asn Pro Gly Asn Asn Asn Asp Lys Gln Phe Ser Leu
 145 150 155 160
 Leu Leu Glu Glu Tyr Arg Ser Leu Phe Gly Leu Ala Ser Leu Arg Phe
 165 170 175
 Gln Gly Asp Gln His Leu Leu Asp Ile Ala Phe Trp Cys Asn Glu Lys
 180 185 190
 Gly Val Ser Ala Arg Gln Gln Leu Ser Val Gln Gln Gln Asn Gly Ile
 195 200 205
 Trp Thr Leu Val Gln Ser Glu Glu Ala Glu Ile Gln Pro Arg Ser Asp
 210 215 220
 Glu Lys Arg Ile Leu Ser Asn Val Ala Val Leu Glu Gly Ala Pro Pro
 225 230 235 240
 Leu Ser Glu His Trp Gln Leu Phe Asn Asn Asn Glu Val Leu Phe Asn
 245 250 255
 Glu Ala Arg Thr Ala Gln Ala Ala Thr Val Val Phe Ser Leu Gln Gln
 260 265 270
 Asn Ala Gln Ile Glu Pro Leu Ala Arg Ser Ile His Thr Leu Arg Arg
 275 280 285
 Gln Arg Gly Ser Ala Met Lys Ile Leu Val Arg Glu Asn Thr Ala Ser
 290 295 300
 Leu Arg Ala Thr Asp Glu Arg Leu Leu Leu Ala Cys Gly Ala Asn Met
 305 310 315 320
 Val Ile Pro Trp Asn Ala Pro Leu Ser Arg Cys Leu Thr Met Ile Glu
 325 330 335
 Ser Val Gln Gly Gln Lys Phe Ser Arg Tyr Val Pro Glu Asp Ile Thr
 340 345 350
 Thr Leu Leu Ser Met Thr Gln Pro Leu Lys Leu Arg Gly Phe Gln Lys
 355 360 365
 Trp Asp Val Phe Cys Asn Ala Val Asn Asn Met Met Asn Asn Pro Leu
 370 375 380
 Leu Pro Ala His Gly Lys Gly Val Leu Val Ala Leu Arg Pro Val Pro
 385 390 395 400
 Gly Ile Arg Val Glu Gln Ala Leu Thr Leu Cys Arg Pro Asn Arg Thr
 405 410 415
 Gly Asp Ile Met Thr Ile Gly Gly Asn Arg Leu Val Leu Phe Leu Ser
 420 425 430
 Phe Cys Arg Ile Asn Asp Leu Asp Thr Ala Leu Asn His Ile Phe Pro
 435 440 445
 Leu Pro Thr Gly Asp Ile Phe Ser Asn Arg Met Val Trp Phe Glu Asp
 450 455 460
 Asp Gln Ile Ser Ala Glu Leu Val Gln Met Arg Leu Leu Ala Pro Glu
 465 470 475 480
 Gln Trp Gly Met Pro Leu Pro Leu Thr Gln Ser Ser Lys Pro Val Ile
 485 490 495
 Asn Ala Glu His Asp Gly Arg His Trp Arg Arg Ile Pro Glu Pro Met
 500 505 510
 Arg Leu Leu Asp Asp Ala Val Glu Arg Ser Ser
 515 520

<210> 330

<211> 62

<212> PRT

<213> E. Coli

<400> 330

```

Met Thr Ile Ser Asp Ile Ile Glu Ile Ile Val Val Cys Ala Leu Ile
 1          5          10          15
Phe Phe Pro Leu Gly Tyr Leu Ala Arg His Ser Leu Arg Arg Ile Arg
          20          25          30
Asp Thr Leu Arg Leu Phe Phe Ala Lys Pro Arg Tyr Val Lys Pro Ala
          35          40          45
Gly Thr Leu Arg Arg Thr Glu Lys Ala Arg Ala Thr Lys Lys
 50          55          60

```

<210> 331

<211> 559

<212> PRT

<213> E. Coli

<400> 331

```

Met Thr Gln Phe Thr Gln Asn Thr Ala Met Pro Ser Ser Leu Trp Gln
 1          5          10          15
Tyr Trp Arg Gly Leu Ser Gly Trp Asn Phe Tyr Phe Leu Val Lys Phe
          20          25          30
Gly Leu Leu Trp Ala Gly Tyr Leu Asn Phe His Pro Leu Leu Asn Leu
          35          40          45
Val Phe Ala Ala Phe Leu Leu Met Pro Leu Pro Arg Tyr Ser Leu His
          50          55          60
Arg Leu Arg His Trp Ile Ala Leu Pro Ile Gly Phe Ala Leu Phe Trp
 65          70          75          80
His Asp Thr Trp Leu Pro Gly Pro Glu Ser Ile Met Ser Gln Gly Ser
          85          90          95
Gln Val Ala Gly Phe Ser Thr Asp Tyr Leu Ile Asp Leu Val Thr Arg
          100          105          110
Phe Ile Asn Trp Gln Met Ile Gly Ala Ile Phe Val Leu Leu Val Ala
          115          120          125
Trp Leu Phe Leu Ser Gln Trp Ile Arg Ile Thr Val Phe Val Val Ala
          130          135          140
Ile Leu Leu Trp Leu Asn Val Leu Thr Leu Ala Gly Pro Ser Phe Ser
 145          150          155          160
Leu Trp Pro Ala Gly Gln Pro Thr Thr Thr Val Thr Thr Thr Gly Gly
          165          170          175
Asn Ala Ala Ala Thr Val Ala Ala Thr Gly Gly Ala Pro Val Val Gly
          180          185          190
Asp Met Pro Ala Gln Thr Ala Pro Pro Thr Thr Ala Asn Leu Asn Ala
          195          200          205
Trp Leu Asn Asn Phe Tyr Asn Ala Glu Ala Lys Arg Lys Ser Thr Phe
          210          215          220
Pro Ser Ser Leu Pro Ala Asp Ala Gln Pro Phe Glu Leu Leu Val Ile
 225          230          235          240
Asn Ile Cys Ser Leu Ser Trp Ser Asp Ile Glu Ala Ala Gly Leu Met
          245          250          255
Ser His Pro Leu Trp Ser His Phe Asp Ile Glu Phe Lys Asn Phe Asn
          260          265          270
Ser Ala Thr Ser Tyr Ser Gly Pro Ala Ala Ile Arg Leu Leu Arg Ala
          275          280          285
Ser Cys Gly Gln Thr Ser His Thr Asn Leu Tyr Gln Pro Ala Asn Asn
          290          295          300
Asp Cys Tyr Leu Phe Asp Asn Leu Ser Lys Leu Gly Phe Thr Gln His
 305          310          315          320
Leu Met Met Gly His Asn Gly Gln Phe Gly Gly Phe Leu Lys Glu Val
          325          330          335

```


Arg Glu Asn Gly Gly Met Gln Ser Glu Leu Met Asp Gln Thr Asn Leu
 340 345 350
 Pro Val Ile Leu Leu Gly Phe Asp Gly Ser Pro Val Tyr Asp Asp Thr
 355 360 365
 Ala Val Leu Asn Arg Trp Leu Asp Val Thr Glu Lys Asp Lys Asn Ser
 370 375 380
 Arg Ser Ala Thr Phe Tyr Asn Thr Leu Pro Leu His Asp Gly Asn His
 385 390 395 400
 Tyr Pro Gly Val Ser Lys Thr Ala Asp Tyr Lys Ala Arg Ala Gln Lys
 405 410 415
 Phe Phe Asp Glu Leu Asp Ala Phe Phe Thr Glu Leu Glu Lys Ser Gly
 420 425 430
 Arg Lys Val Met Val Val Val Val Pro Glu His Gly Gly Ala Leu Lys
 435 440 445
 Gly Asp Arg Met Gln Val Ser Gly Leu Arg Asp Ile Pro Ser Pro Ser
 450 455 460
 Ile Thr Asp Val Pro Val Gly Val Lys Phe Phe Gly Met Lys Ala Pro
 465 470 475 480
 His Gln Gly Ala Pro Ile Val Ile Glu Gln Pro Ser Ser Phe Leu Ala
 485 490 495
 Ile Ser Asp Leu Val Val Arg Val Leu Asp Gly Lys Ile Phe Thr Glu
 500 505 510
 Asp Asn Val Asp Trp Lys Lys Leu Thr Ser Gly Leu Pro Gln Thr Ala
 515 520 525
 Pro Val Ser Glu Asn Ser Asn Ala Val Val Ile Gln Tyr Gln Asp Lys
 530 535 540
 Pro Tyr Val Arg Leu Asn Gly Gly Asp Trp Val Pro Tyr Pro Gln
 545 550 555

<210> 332
 <211> 127
 <212> PRT
 <213> E. Coli

<400> 332
 Met Glu Gly Ser Arg Met Lys Tyr Arg Ile Ala Leu Ala Val Ser Leu
 1 5 10 15
 Phe Ala Leu Ser Ala Gly Ser Tyr Ala Thr Thr Leu Cys Gln Glu Lys
 20 25 30
 Glu Gln Asn Ile Leu Lys Glu Ile Ser Tyr Ala Glu Lys His Gln Asn
 35 40 45
 Gln Asn Arg Ile Asp Gly Leu Asn Lys Ala Leu Ser Glu Val Arg Ala
 50 55 60
 Asn Cys Ser Asp Ser Gln Leu Arg Ala Asp His Gln Lys Lys Ile Ala
 65 70 75 80
 Lys Gln Lys Asp Glu Val Ala Glu Arg Gln Gln Asp Leu Ala Glu Ala
 85 90 95
 Lys Gln Lys Gly Asp Ala Asp Lys Ile Ala Lys Arg Glu Arg Lys Leu
 100 105 110
 Ala Glu Ala Gln Glu Glu Leu Lys Lys Leu Glu Ala Arg Asp Tyr
 115 120 125

<210> 333
 <211> 101
 <212> PRT
 <213> E. Coli

<400> 333
 Met Ser Lys Glu His Thr Thr Glu His Leu Arg Ala Glu Leu Lys Ser


```

1           5           10           15
Leu Ser Asp Thr Leu Glu Glu Val Leu Ser Ser Ser Gly Glu Lys Ser
20
Lys Glu Glu Leu Ser Lys Ile Arg Ser Lys Ala Glu Gln Ala Leu Lys
35
Gln Ser Arg Tyr Arg Leu Gly Glu Thr Gly Asp Ala Ile Ala Lys Gln
50
Thr Arg Val Ala Ala Ala Arg Ala Asp Glu Tyr Val Arg Glu Asn Pro
65
Trp Thr Gly Val Gly Ile Gly Ala Ala Ile Gly Val Val Leu Gly Val
85
Leu Leu Ser Arg Arg
100

```

<210> 334

<211> 134

<212> PRT

<213> E. Coli

<400> 334

```

Met Ala Asp Thr His His Ala Gln Gly Pro Gly Lys Ser Val Leu Gly
1           5           10           15
Ile Gly Gln Arg Ile Val Ser Ile Met Val Glu Met Val Glu Thr Arg
20
Leu Arg Leu Ala Val Val Glu Leu Glu Glu Glu Lys Ala Asn Leu Phe
35
Gln Leu Leu Leu Met Leu Gly Leu Thr Met Leu Phe Ala Ala Phe Gly
50
Leu Met Ser Leu Met Val Leu Ile Ile Trp Ala Val Asp Pro Gln Tyr
65
Arg Leu Asn Ala Met Ile Ala Thr Thr Val Val Leu Leu Leu Leu Ala
85
Leu Ile Gly Gly Ile Trp Thr Leu Arg Lys Ser Arg Lys Ser Thr Leu
100
Leu Arg His Thr Arg His Glu Leu Ala Asn Asp Arg Gln Leu Leu Glu
115
Glu Glu Ser Arg Glu Gln
130

```

<210> 335

<211> 99

<212> PRT

<213> E. Coli

<400> 335

```

Met Ser Ser Lys Val Glu Arg Glu Arg Arg Lys Ala Gln Leu Leu Ser
1           5           10           15
Gln Ile Gln Gln Arg Leu Asp Leu Ser Ala Ser Arg Arg Glu Trp
20
Leu Glu Thr Thr Gly Ala Tyr Asp Arg Arg Trp Asn Met Leu Leu Ser
35
Leu Arg Ser Trp Ala Leu Val Gly Ser Ser Val Met Ala Ile Trp Thr
50
Ile Arg His Pro Asn Met Leu Val Arg Trp Ala Arg Arg Gly Phe Gly
65
Val Trp Ser Ala Trp Arg Leu Val Lys Thr Thr Leu Lys Gln Gln Gln
85
Leu Arg Gly
90

```


<210> 336
 <211> 160
 <212> PRT
 <213> E. Coli

<400> 336
 Met Ile Leu Ser Ile Asp Ser Asn Asp Ala Asn Thr Ala Pro Leu His
 1 5 10 15
 Lys Lys Thr Ile Ser Ser Leu Ser Gly Ala Val Glu Ser Met Met Lys
 20 25 30
 Lys Leu Glu Asp Val Gly Val Leu Val Ala Arg Ile Leu Met Pro Ile
 35 40 45
 Leu Phe Ile Thr Ala Gly Trp Gly Lys Ile Thr Gly Tyr Ala Gly Thr
 50 55 60
 Gln Gln Tyr Met Glu Ala Met Gly Val Pro Gly Phe Met Leu Pro Leu
 65 70 75 80
 Val Ile Leu Leu Glu Phe Gly Gly Gly Leu Ala Ile Leu Phe Gly Phe
 85 90 95
 Leu Thr Arg Thr Thr Ala Leu Phe Thr Ala Gly Phe Thr Leu Leu Thr
 100 105 110
 Ala Phe Leu Phe His Ser Asn Phe Ala Glu Gly Val Asn Ser Leu Met
 115 120 125
 Phe Met Lys Asn Leu Thr Ile Ser Gly Gly Phe Leu Leu Leu Ala Ile
 130 135 140
 Thr Gly Pro Gly Ala Tyr Ser Ile Asp Arg Leu Leu Asn Lys Lys Trp
 145 150 155 160

<210> 337
 <211> 296
 <212> PRT
 <213> E. Coli

<400> 337
 Met Ile Lys Lys Thr Thr Glu Ile Asp Ala Ile Leu Leu Asn Leu Asn
 1 5 10 15
 Lys Ala Ile Asp Ala His Tyr Gln Trp Leu Val Ser Met Phe His Ser
 20 25 30
 Val Val Ala Arg Asp Ala Ser Lys Pro Glu Ile Thr Asp Asn His Ser
 35 40 45
 Tyr Gly Leu Cys Gln Phe Gly Arg Trp Ile Asp His Leu Gly Pro Leu
 50 55 60
 Asp Asn Asp Glu Leu Pro Tyr Val Arg Leu Met Asp Ser Ala His Gln
 65 70 75 80
 His Met His Asn Cys Gly Arg Glu Leu Met Leu Ala Ile Val Glu Asn
 85 90 95
 His Trp Gln Asp Ala His Phe Asp Ala Phe Gln Glu Gly Leu Leu Ser
 100 105 110
 Phe Thr Ala Ala Leu Thr Asp Tyr Lys Ile Tyr Leu Leu Thr Ile Arg
 115 120 125
 Ser Asn Met Asp Val Leu Thr Gly Leu Pro Gly Arg Arg Val Leu Asp
 130 135 140
 Glu Ser Phe Asp His Gln Leu Arg Asn Ala Glu Pro Leu Asn Leu Tyr
 145 150 155 160
 Leu Met Leu Leu Asp Ile Asp Arg Phe Lys Leu Val Asn Asp Thr Tyr
 165 170 175

Gly His Leu Ile Gly Asp Val Val Leu Arg Thr Leu Ala Thr Tyr Leu
 180 185 190
 Ala Ser Trp Thr Arg Asp Tyr Glu Thr Val Tyr Arg Tyr Gly Gly Glu
 195 200 205
 Glu Phe Ile Ile Ile Val Lys Ala Ala Asn Asp Glu Glu Ala Cys Arg
 210 215 220
 Ala Gly Val Arg Ile Cys Gln Leu Val Asp Asn His Ala Ile Thr His
 225 230 235 240
 Ser Glu Gly His Ile Asn Ile Thr Val Thr Ala Gly Val Ser Arg Ala
 245 250 255
 Phe Pro Glu Glu Pro Leu Asp Val Val Ile Gly Arg Ala Asp Arg Ala
 260 265 270
 Met Tyr Glu Gly Lys Gln Thr Gly Arg Asn Arg Cys Met Phe Ile Asp
 275 280 285
 Glu Gln Asn Val Ile Asn Arg Val
 290 295

<210> 338
 <211> 203
 <212> PRT
 <213> E. Coli

<400> 338
 Met Arg Leu Arg Val Val Pro Gly Phe Ile Ser Pro Pro Pro Gly Phe
 1 5 10 15
 Gly Gly Leu Gly Tyr Thr Pro Thr Ala Arg Ala Cys Val Asn Ile Ser
 20 25 30
 Ile Pro Leu Gln Leu Arg Val Ile Asp Met Leu Asp Val Phe Thr Pro
 35 40 45
 Leu Leu Lys Leu Phe Ala Asn Glu Pro Leu Glu Arg Leu Met Tyr Thr
 50 55 60
 Ile Ile Ile Phe Gly Leu Thr Leu Trp Leu Ile Pro Lys Glu Phe Thr
 65 70 75 80
 Val Ala Phe Asn Ala Tyr Thr Glu Ile Pro Trp Leu Phe Gln Ile Ile
 85 90 95
 Val Phe Ala Phe Ser Phe Val Val Ala Ile Ser Phe Ser Arg Leu Arg
 100 105 110
 Ala His Ile Gln Lys His Tyr Ser Leu Leu Pro Glu Gln Arg Val Leu
 115 120 125
 Leu Arg Leu Ser Glu Lys Glu Ile Ala Val Phe Lys Asp Phe Leu Lys
 130 135 140
 Thr Gly Asn Leu Ile Ile Thr Ser Pro Cys Arg Asn Pro Val Met Lys
 145 150 155 160
 Lys Leu Glu Arg Lys Gly Ile Ile Gln His Gln Ser Asp Ser Ala Asn
 165 170 175
 Cys Ser Tyr Tyr Leu Val Thr Glu Lys Tyr Ser His Phe Met Lys Leu
 180 185 190
 Phe Trp Asn Ser Arg Ser Arg Arg Phe Asn Arg
 195 200

<210> 339
 <211> 58
 <212> PRT
 <213> E. Coli

<400> 339
 Met Leu Leu Gln Pro Ser Ala Arg Thr Ser Phe Gly Phe Lys Cys Phe

1 5 10 15
 Ala Phe Gly Ile Arg His Gly Ser Glu Arg Ser Ile Leu Val Gly Glu
 20 25 30
 His Ala Ala His Gln Gly Phe Val Val Ala Glu Val Asp Phe Leu His
 35 40 45
 Phe Ala Asn Leu Thr Ser Cys Cys Tyr Val
 50 55

<210> 340
 <211> 1426
 <212> PRT
 <213> E. Coli

<400> 340
 Met Ser Gly Lys Pro Ala Ala Arg Gln Gly Asp Met Thr Gln Tyr Gly
 1 5 10 15
 Gly Pro Ile Val Gln Gly Ser Ala Gly Val Arg Ile Gly Ala Pro Thr
 20 25 30
 Gly Val Ala Cys Ser Val Cys Pro Gly Gly Met Thr Ser Gly Asn Pro
 35 40 45
 Val Asn Pro Leu Leu Gly Ala Lys Val Leu Pro Gly Glu Thr Asp Leu
 50 55 60
 Ala Leu Pro Gly Pro Leu Pro Phe Ile Leu Ser Arg Thr Tyr Ser Ser
 65 70 75 80
 Tyr Arg Thr Lys Thr Pro Ala Pro Val Gly Val Phe Gly Pro Gly Trp
 85 90 95
 Lys Ala Pro Ser Asp Ile Arg Leu Gln Leu Arg Asp Asp Gly Leu Ile
 100 105 110
 Leu Asn Asp Asn Gly Gly Arg Ser Ile His Phe Glu Pro Leu Leu Pro
 115 120 125
 Gly Glu Ala Val Tyr Ser Arg Ser Glu Ser Met Trp Leu Val Arg Gly
 130 135 140
 Gly Lys Ala Ala Gln Pro Asp Gly His Thr Leu Ala Arg Leu Trp Gly
 145 150 155 160
 Ala Leu Pro Pro Asp Ile Arg Leu Ser Pro His Leu Tyr Leu Ala Thr
 165 170 175
 Asn Ser Ala Gln Gly Pro Trp Trp Ile Leu Gly Trp Ser Glu Arg Val
 180 185 190
 Pro Gly Ala Glu Asp Val Leu Pro Ala Pro Leu Pro Pro Tyr Arg Val
 195 200 205
 Leu Thr Gly Met Ala Asp Arg Phe Gly Arg Thr Leu Thr Tyr Arg Arg
 210 215 220
 Glu Ala Ala Gly Asp Leu Ala Gly Glu Ile Thr Gly Val Thr Asp Gly
 225 230 235 240
 Ala Gly Arg Glu Phe Arg Leu Val Leu Thr Thr Gln Ala Gln Arg Ala
 245 250 255
 Glu Glu Ala Arg Thr Ser Ser Leu Ser Ser Ser Asp Ser Ser Arg Pro
 260 265 270
 Leu Ser Ala Ser Ala Phe Pro Asp Thr Leu Pro Gly Thr Glu Tyr Gly
 275 280 285
 Pro Asp Arg Gly Ile Arg Leu Ser Ala Val Trp Leu Met His Asp Pro
 290 295 300
 Ala Tyr Pro Glu Ser Leu Pro Ala Ala Pro Leu Val Arg Tyr Thr Tyr
 305 310 315 320
 Thr Glu Ala Gly Glu Leu Leu Ala Val Tyr Asp Arg Ser Asn Thr Gln
 325 330 335
 Val Arg Ala Phe Thr Tyr Asp Ala Gln His Pro Gly Arg Met Val Ala
 340 345 350
 His Arg Tyr Ala Gly Arg Pro Glu Met Arg Tyr Arg Tyr Asp Asp Thr
 355 360 365

Gly Arg Val Val Glu Gln Leu Asn Pro Ala Gly Leu Ser Tyr Arg Tyr
 370 375 380
 Leu Tyr Glu Gln Asp Arg Ile Thr Val Thr Asp Ser Leu Asn Arg Arg
 385 390 395 400
 Glu Val Leu His Thr Glu Gly Gly Ala Gly Leu Lys Arg Val Val Lys
 405 410 415
 Lys Glu Leu Ala Asp Gly Ser Val Thr Arg Ser Gly Tyr Asp Ala Ala
 420 425 430
 Gly Arg Leu Thr Ala Gln Thr Asp Ala Ala Gly Arg Arg Thr Glu Tyr
 435 440 445
 Gly Leu Asn Val Val Ser Gly Asp Ile Thr Asp Ile Thr Thr Pro Asp
 450 455 460
 Gly Arg Glu Thr Lys Phe Tyr Tyr Asn Asp Gly Asn Gln Leu Thr Ala
 465 470 475 480
 Val Val Ser Pro Asp Gly Leu Glu Ser Arg Arg Glu Tyr Asp Glu Pro
 485 490 495
 Gly Arg Leu Val Ser Glu Thr Ser Arg Ser Gly Glu Thr Val Arg Tyr
 500 505 510
 Arg Tyr Asp Asp Ala His Ser Glu Leu Pro Ala Thr Thr Thr Asp Ala
 515 520 525
 Thr Gly Ser Thr Arg Gln Met Thr Trp Ser Arg Tyr Gly Gln Leu Leu
 530 535 540
 Ala Phe Thr Asp Cys Ser Gly Tyr Gln Thr Arg Tyr Glu Tyr Asp Arg
 545 550 555 560
 Phe Gly Gln Met Thr Ala Val His Arg Glu Glu Gly Ile Ser Leu Tyr
 565 570 575
 Arg Arg Tyr Asp Asn Arg Gly Arg Leu Thr Ser Val Lys Asp Ala Gln
 580 585 590
 Gly Arg Glu Thr Arg Tyr Glu Tyr Asn Ala Ala Gly Asp Leu Thr Ala
 595 600 605
 Val Ile Thr Pro Asp Gly Asn Arg Ser Glu Thr Gln Tyr Asp Ala Trp
 610 615 620
 Gly Lys Ala Val Ser Thr Thr Gln Gly Gly Leu Thr Arg Ser Met Glu
 625 630 635 640
 Tyr Asp Ala Ala Gly Arg Val Ile Ser Leu Thr Asn Glu Asn Gly Ser
 645 650 655
 His Ser Val Phe Ser Tyr Asp Ala Leu Asp Arg Leu Val Gln Gln Gly
 660 665 670
 Gly Phe Asp Gly Arg Thr Gln Arg Tyr His Tyr Asp Leu Thr Gly Lys
 675 680 685
 Leu Thr Gln Ser Glu Asp Glu Gly Leu Val Ile Leu Trp Tyr Tyr Asp
 690 695 700
 Glu Ser Asp Arg Ile Thr His Arg Thr Val Asn Gly Glu Pro Ala Glu
 705 710 715 720
 Gln Trp Gln Tyr Asp Gly His Gly Trp Leu Thr Asp Ile Ser His Leu
 725 730 735
 Ser Glu Gly His Arg Val Ala Val His Tyr Gly Tyr Asp Asp Lys Gly
 740 745 750
 Arg Leu Thr Gly Glu Cys Gln Thr Val Glu Asn Pro Glu Thr Gly Glu
 755 760 765
 Leu Leu Trp Gln His Glu Thr Lys His Ala Tyr Asn Glu Gln Gly Leu
 770 775 780
 Ala Asn Arg Val Thr Pro Asp Ser Leu Pro Pro Val Glu Trp Leu Thr
 785 790 795 800
 Tyr Gly Ser Gly Tyr Leu Ala Gly Met Lys Leu Gly Gly Thr Pro Leu
 805 810 815
 Val Glu Tyr Thr Arg Asp Arg Leu His Arg Glu Thr Val Arg Ser Phe
 820 825 830
 Gly Ser Met Ala Gly Ser Asn Ala Ala Tyr Glu Leu Thr Ser Thr Tyr
 835 840 845
 Thr Pro Ala Gly Gln Leu Gln Ser Gln His Leu Asn Ser Leu Val Tyr

850	855	860
Asp Arg Asp Tyr Gly Trp Ser Asp Asn Gly Asp Leu Val Arg Ile Ser		
865	870	875
Gly Pro Arg Gln Thr Arg Glu Tyr Gly Tyr Ser Ala Thr Gly Arg Leu		880
	885	890
Glu Ser Val Arg Thr Leu Ala Pro Asp Leu Asp Ile Arg Ile Pro Tyr		895
	900	905
Ala Thr Asp Pro Ala Gly Asn Arg Leu Pro Asp Pro Glu Leu His Pro		910
	915	920
Asp Ser Thr Leu Thr Val Trp Pro Asp Asn Arg Ile Ala Glu Asp Ala		925
930	935	940
His Tyr Val Tyr Arg His Asp Glu Tyr Gly Arg Leu Thr Glu Lys Thr		
945	950	955
Asp Arg Ile Pro Ala Gly Val Ile Arg Thr Asp Asp Glu Arg Thr His		960
	965	970
His Tyr His Tyr Asp Ser Gln His Arg Leu Val Phe Tyr Thr Arg Ile		975
	980	985
Gln His Gly Glu Pro Leu Val Glu Ser Arg Tyr Leu Tyr Asp Pro Leu		990
	995	1000
Gly Arg Arg Met Ala Lys Arg Val Trp Arg Arg Glu Arg Asp Leu Thr		1005
1010	1015	1020
Gly Trp Met Ser Leu Ser Arg Lys Pro Glu Val Thr Trp Tyr Gly Trp		
1025	1030	1035
Asp Gly Asp Arg Leu Thr Thr Val Gln Thr Asp Thr Thr Arg Ile Gln		1040
	1045	1050
Thr Val Tyr Glu Pro Gly Ser Phe Thr Pro Leu Ile Arg Val Glu Thr		1055
	1060	1065
Glu Asn Gly Glu Arg Glu Lys Ala Gln Arg Arg Ser Leu Ala Glu Thr		1070
1075	1080	1085
Leu Gln Gln Glu Gly Ser Glu Asn Gly His Gly Val Val Phe Pro Ala		
1090	1095	1100
Glu Leu Val Arg Leu Leu Asp Arg Leu Glu Glu Glu Ile Arg Ala Asp		
1105	1110	1115
Arg Val Ser Ser Glu Ser Arg Ala Trp Leu Ala Gln Cys Gly Leu Thr		1120
	1125	1130
Val Glu Gln Leu Ala Arg Gln Val Glu Pro Glu Tyr Thr Pro Ala Arg		1135
	1140	1145
Lys Ala His Leu Tyr His Cys Asp His Arg Gly Leu Pro Leu Ala Leu		1150
	1155	1160
Ile Ser Glu Asp Gly Asn Thr Ala Trp Ser Ala Glu Tyr Asp Glu Trp		1165
1170	1175	1180
Gly Asn Gln Leu Asn Glu Glu Asn Pro His His Val Tyr Gln Pro Tyr		
1185	1190	1195
Arg Leu Pro Gly Gln Gln His Asp Glu Glu Ser Gly Leu Tyr Tyr Asn		1200
	1205	1210
Arg His Arg Tyr Tyr Asp Pro Leu Gln Gly Arg Tyr Ile Thr Gln Asp		1215
	1220	1225
Pro Met Gly Leu Lys Gly Gly Trp Asn Leu Tyr Gln Tyr Pro Leu Asn		1230
1235	1240	1245
Pro Leu Gln Gln Ile Asp Pro Met Gly Leu Leu Gln Thr Trp Asp Asp		
1250	1255	1260
Ala Arg Ser Gly Ala Cys Thr Gly Gly Val Cys Gly Val Leu Ser Arg		
1265	1270	1275
Ile Ile Gly Pro Ser Lys Phe Asp Ser Thr Ala Asp Ala Ala Leu Asp		1280
	1285	1290
Ala Leu Lys Glu Thr Gln Asn Arg Ser Leu Cys Asn Asp Met Glu Tyr		1295
	1300	1305
Ser Gly Ile Val Cys Lys Asp Thr Asn Gly Lys Tyr Phe Ala Ser Lys		1310
	1315	1320
Ala Glu Thr Asp Asn Leu Arg Lys Glu Ser Tyr Pro Leu Lys Arg Lys		1325
1330	1335	1340

Cys Pro Thr Gly Thr Asp Arg Val Ala Ala Tyr His Thr His Gly Ala
 1345 1350 1355 1360
 Asp Ser His Gly Asp Tyr Val Asp Glu Phe Phe Ser Ser Ser Asp Lys
 1365 1370 1375
 Asn Leu Val Arg Ser Lys Asp Asn Asn Leu Glu Ala Phe Tyr Leu Ala
 1380 1385 1390
 Thr Pro Asp Gly Arg Phe Glu Ala Leu Asn Asn Lys Gly Glu Tyr Ile
 1395 1400 1405
 Phe Ile Arg Asn Ser Val Pro Gly Leu Ser Ser Val Cys Ile Pro Tyr
 1410 1415 1420
 His Asp
 1425

<210> 341
 <211> 122
 <212> PRT
 <213> E. Coli

<400> 341
 Met Lys Tyr Ser Ser Ile Phe Ser Met Leu Ser Phe Phe Ile Leu Phe
 1 5 10 15
 Ala Cys Asn Glu Thr Ala Val Tyr Gly Ser Asp Glu Asn Ile Ile Phe
 20 25 30
 Met Arg Tyr Val Glu Lys Leu His Leu Asp Lys Tyr Ser Val Lys Asn
 35 40 45
 Thr Val Lys Thr Glu Thr Met Ala Ile Gln Leu Ala Glu Ile Tyr Val
 50 55 60
 Arg Tyr Arg Tyr Gly Glu Arg Ile Ala Glu Glu Glu Lys Pro Tyr Leu
 65 70 75 80
 Ile Thr Glu Leu Pro Asp Ser Trp Val Val Glu Gly Ala Lys Leu Pro
 85 90 95
 Tyr Glu Val Ala Gly Gly Val Phe Ile Ile Glu Ile Asn Lys Lys Asn
 100 105 110
 Gly Cys Val Leu Asn Phe Leu His Ser Lys
 115 120

<210> 342
 <211> 236
 <212> PRT
 <213> E. Coli

<400> 342
 Met Leu Ala Leu Met Asp Ala Asp Gly Asn Ile Ala Trp Ser Gly Glu
 1 5 10 15
 Tyr Asp Glu Trp Gly Asn Gln Leu Asn Glu Glu Asn Pro His His Leu
 20 25 30
 His Gln Pro Tyr Arg Leu Pro Gly Gln Gln Tyr Asp Lys Glu Ser Gly
 35 40 45
 Leu Tyr Tyr Asn Arg Asn Arg Tyr Tyr Asp Pro Leu Gln Gly Arg Tyr
 50 55 60
 Ile Thr Gln Asp Pro Ile Gly Leu Glu Gly Gly Trp Ser Leu Tyr Ala
 65 70 75 80
 Tyr Pro Leu Asn Pro Val Asn Gly Ile Asp Pro Leu Gly Leu Ser Pro
 85 90 95
 Ala Asp Val Ala Leu Ile Arg Arg Lys Asp Gln Leu Asn His Gln Arg
 100 105 110
 Ala Trp Asp Ile Leu Ser Asp Thr Tyr Glu Asp Met Lys Arg Leu Asn
 115 120 125
 Leu Gly Gly Thr Asp Gln Phe Phe His Cys Met Ala Phe Cys Arg Val


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      130              135              140
Ser Lys Leu Asn Asp Ala Gly Val Ser Arg Ser Ala Lys Gly Leu Gly
145              150              155              160
Tyr Glu Lys Glu Ile Arg Asp Tyr Gly Leu Asn Leu Phe Gly Met Tyr
      165              170              175
Gly Arg Lys Val Lys Leu Ser His Ser Glu Met Ile Glu Asp Asn Lys
      180              185              190
Lys Asp Leu Ala Val Asn Asp His Gly Leu Thr Cys Pro Ser Thr Thr
      195              200              205
Asp Cys Ser Asp Arg Cys Ser Asp Tyr Ile Asn Pro Glu His Lys Lys
      210              215              220
Thr Ile Lys Ala Leu Gln Asp Ala Gly Tyr Leu Lys
225              230              235

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<210> 343
 <211> 86
 <212> PRT
 <213> E. Coli

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      <400> 343
Met Leu Ala Ile Ser Ser Asn Leu Ser Lys Met Ile Ile Phe Ile Phe
 1              5              10              15
Ala Ile Ile Ile Val Val Leu Cys Val Ile Thr Tyr Leu Tyr Leu
      20              25              30
Tyr Lys Asp Glu Ser Leu Val Ser Lys His Tyr Ile Asn Tyr Met Ala
      35              40              45
Ile Pro Glu Asn Asp Gly Val Phe Thr Trp Leu Pro Asp Phe Phe Pro
      50              55              60
His Val Ala Val Asp Ile Ser Ile Tyr Thr Asn Val Glu Asp Asp Tyr
65              70              75              80
Phe Phe Leu Ile Phe Pro
      85

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<210> 344
 <211> 63
 <212> PRT
 <213> E. Coli

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      <400> 344
Met Arg Ala Arg Glu Gln Val Ala Lys Ile Val Ser Lys Asn Asp Pro
 1              5              10              15
Asp Thr Lys Lys Val Trp Cys Lys Tyr Gly Lys Ile Pro Gly Gln Gly
      20              25              30
Asp Gly Val Asn Leu Phe Phe Val Gly Glu Ile Asn Val Thr His Tyr
      35              40              45
Phe Ile Thr Asn Ile Gly Ala Gly Leu Pro Asp Ala Cys Ala Glu
50              55              60

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<210> 345
 <211> 167
 <212> PRT
 <213> E. Coli

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      <400> 345
Met Pro Gly Asn Ser Pro His Tyr Gly Arg Trp Pro Gln His Asp Phe
 1              5              10              15

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Thr Ser Leu Lys Lys Leu Arg Pro Gln Ser Val Thr Ser Arg Ile Gln
 20 25 30
 Pro Gly Ser Asp Val Ile Val Cys Ala Glu Met Asp Glu Gln Trp Gly
 35 40 45
 Tyr Val Gly Ala Lys Ser Arg Gln Arg Trp Leu Phe Tyr Ala Tyr Asp
 50 55 60
 Ser Leu Arg Lys Thr Val Val Ala His Val Phe Gly Glu Arg Thr Met
 65 70 75 80
 Ala Thr Leu Gly Arg Leu Met Ser Leu Leu Ser Pro Phe Asp Val Val
 85 90 95
 Ile Trp Met Thr Asp Gly Trp Pro Leu Tyr Glu Ser Arg Leu Lys Gly
 100 105 110
 Lys Leu His Val Ile Ser Lys Arg Tyr Thr Gln Arg Ile Glu Arg His
 115 120 125
 Asn Leu Asn Leu Arg Gln His Leu Ala Arg Leu Gly Arg Lys Ser Leu
 130 135 140
 Ser Phe Ser Lys Ser Val Glu Leu His Asp Lys Val Ile Gly His Tyr
 145 150 155 160
 Leu Asn Ile Lys His Tyr Gln
 165

<210> 346
 <211> 91
 <212> PRT
 <213> E. Coli

<400> 346
 Met Ala Ser Val Ser Ile Ser Cys Pro Ser Cys Ser Ala Thr Asp Gly
 1 5 10 15
 Val Val Arg Asn Gly Lys Ser Thr Ala Gly His Gln Arg Tyr Leu Cys
 20 25 30
 Ser His Cys Arg Lys Thr Trp Gln Leu Gln Phe Thr Tyr Thr Ala Ser
 35 40 45
 Gln Pro Gly Thr His Gln Lys Ile Ile Asp Met Ala Met Asn Gly Val
 50 55 60
 Gly Cys Arg Ala Thr Ala Arg Ile Met Gly Val Gly Leu Asn Thr Ile
 65 70 75 80
 Leu Arg His Leu Lys Asn Ser Gly Arg Ser Arg
 85 90

<210> 347
 <211> 138
 <212> PRT
 <213> E. Coli

<400> 347
 Met Met Thr Lys Thr Gln Ile Asn Lys Leu Ile Lys Met Met Asn Asp
 1 5 10 15
 Leu Asp Tyr Pro Phe Glu Ala Pro Leu Lys Glu Ser Phe Ile Glu Ser
 20 25 30
 Ile Ile Gln Ile Glu Phe Asn Ser Asn Ser Thr Asn Cys Leu Glu Lys
 35 40 45
 Leu Cys Asn Glu Val Ser Ile Leu Phe Lys Asn Gln Pro Asp Tyr Leu
 50 55 60
 Thr Phe Leu Arg Ala Met Asp Gly Phe Glu Val Asn Gly Leu Arg Leu
 65 70 75 80
 Phe Ser Leu Ser Ile Pro Glu Pro Ser Val Lys Asn Leu Phe Ala Val
 85 90 95

Asn Glu Phe Tyr Arg Asn Asn Asp Asp Phe Ile Asn Pro Asp Leu Gln
 100 105 110
 Glu Arg Leu Val Ile Gly Asp Tyr Ser Ile Ser Ile Phe Thr Tyr Asp
 115 120 125
 Ile Lys Gly Asp Ala Ala Asn Leu Leu Ile
 130 135

<210> 348
 <211> 392
 <212> PRT
 <213> E. Coli

<400> 348
 Met Ser Asn Ile Val Tyr Leu Thr Val Thr Gly Glu Gln Gln Gly Ser
 1 5 10 15
 Ile Ser Ala Gly Cys Gly Thr Ser Glu Ser Thr Gly Asn Arg Trp Gln
 20 25 30
 Ser Gly His Glu Asp Glu Ile Phe Thr Phe Ser Leu Leu Asn Asn Ile
 35 40 45
 Asn Asn Thr Gly Leu Gly Ser Gln Phe His Gly Ile Thr Phe Cys Lys
 50 55 60
 Leu Ile Asp Lys Ser Thr Pro Leu Phe Ile Asn Ser Ile Asn Asn Asn
 65 70 75 80
 Glu Gln Leu Phe Met Gly Phe Asp Phe Tyr Arg Ile Asn Arg Phe Gly
 85 90 95
 Arg Leu Glu Lys Tyr Tyr Tyr Ile Gln Leu Arg Gly Ala Phe Leu Ser
 100 105 110
 Ala Ile His His Gln Ile Ile Glu Asn Gln Leu Asp Thr Glu Thr Ile
 115 120 125
 Thr Ile Ser Tyr Glu Phe Ile Leu Cys Gln His Leu Ile Ala Asn Thr
 130 135 140
 Glu Phe Ser Tyr Leu Ala Leu Pro Glu Asn Tyr Asn Arg Leu Phe Leu
 145 150 155 160
 Pro Asn Ser Lys Asn Gln Thr Asn Asn Arg Phe Lys Thr Leu Asn Ser
 165 170 175
 Lys Ala Ile Gly Arg Leu Leu Ala Ala Gly Gly Val Tyr Asn Gly Asn
 180 185 190
 Ile Glu Gly Phe Arg Asp Thr Ala Glu Lys Leu Gly Gly Asp Ala Ile
 195 200 205
 Lys Gly Tyr Asp Gln Ile Leu Asn Glu Lys Thr Ala Gly Ile Ala Ile
 210 215 220
 Ala Thr Ala Ser Ile Leu Leu Thr Lys Arg Ser Asn Val Asp Thr Tyr
 225 230 235 240
 Thr Glu Ile Asn Ser Tyr Leu Gly Lys Leu Arg Gly Gln Gln Lys Leu
 245 250 255
 Leu Asp Gly Ile Asp Ile Ile Glu Ile Ile Tyr Ile Lys Arg Pro Ser
 260 265 270
 Lys Asp Leu Ala Asn Leu Arg Lys Glu Phe Asn Lys Thr Val Arg Lys
 275 280 285
 Asn Phe Leu Ile Lys Leu Ala Lys Thr Ser Glu Ala Ser Gly Arg Phe
 290 295 300
 Asn Ala Glu Asp Leu Leu Arg Met Arg Lys Gly Asn Val Pro Leu Asn
 305 310 315 320
 Tyr Asn Val His His Lys Leu Ser Leu Asp Asp Gly Gly Thr Asn Asp
 325 330 335
 Phe Glu Asn Leu Val Leu Ile Glu Asn Glu Pro Tyr His Lys Val Phe
 340 345 350
 Thr Asn Met Gln Ser Arg Ile Ala Lys Gly Ile Leu Val Gly Glu Ser
 355 360 365
 Lys Ile Thr Pro Trp Ala Ile Pro Ser Gly Ser Ile Tyr Pro Pro Met

370 375 380
 Lys Asn Ile Met Asp His Thr Lys
 385 390

<210> 349
 <211> 221
 <212> PRT
 <213> E. Coli

<400> 349
 Met Val Leu Ala Leu Asn Tyr Asn Met His Gly Val Asn Ile Arg Ser
 1 5 10 15
 Glu Asn Ala Ala Lys Pro His Thr Met Pro Ser Arg Tyr Leu Cys Glu
 20 25 30
 Tyr Ile Arg Ser Ile Glu Lys Asn Gly His Ala Leu Asp Phe Gly Cys
 35 40 45
 Gly Lys Leu Arg Tyr Ser Asp Glu Leu Ile Ser Lys Phe Asp Glu Val
 50 55 60
 Thr Phe Leu Asp Ser Lys Arg Gln Leu Glu Arg Glu Gln Ile Ile Arg
 65 70 75 80
 Gly Ile Lys Thr Lys Ile Ile Asp Tyr Val Pro Arg Tyr Tyr Lys Asn
 85 90 95
 Ala Asn Thr Val Ala Phe Glu Asp Val Asp Lys Ile Ile Gly Gly Tyr
 100 105 110
 Asp Phe Ile Leu Cys Ser Asn Val Leu Ser Ala Val Pro Cys Arg Asp
 115 120 125
 Thr Ile Asp Lys Ile Val Leu Ser Ile Lys Arg Leu Leu Lys Ser Gly
 130 135 140
 Gly Glu Thr Leu Ile Val Asn Gln Tyr Lys Ser Tyr Phe Lys Lys
 145 150 155 160
 Tyr Glu Thr Gly Arg Lys His Leu Tyr Gly Tyr Ile Tyr Lys Asn Ser
 165 170 175
 Lys Ser Val Ser Tyr Tyr Gly Leu Leu Asp Glu Leu Ala Val Gln Glu
 180 185 190
 Ile Cys Ser Ser His Gly Leu Glu Ile Leu Lys Ser Trp Ser Lys Ala
 195 200 205
 Gly Ser Ser Tyr Val Thr Val Gly Ser Cys Asn Ala Ile
 210 215 220

<210> 350
 <211> 234
 <212> PRT
 <213> E. Coli

<400> 350
 Met Asn Asn Met Phe Glu Pro Pro Lys Asn Tyr Asn Glu Met Leu Pro
 1 5 10 15
 Lys Leu His Lys Ala Thr Phe Leu Asn Thr Leu Ile Tyr Cys Ile Leu
 20 25 30
 Leu Val Ile Tyr Glu Tyr Ile Pro Leu Ile Thr Leu Pro Thr Lys Tyr
 35 40 45
 Val Pro Pro Ile Lys Asp His Glu Ser Phe Ile Asn Trp Ala Leu Ser
 50 55 60
 Phe Gly Ile Leu Pro Cys Ala Phe Ala Ile Phe Ala Tyr Leu Ile Ser
 65 70 75 80
 Gly Ala Leu Asp Leu His Asn Asn Ala Ala Lys Leu Leu Arg Val Arg
 85 90 95
 Tyr Leu Trp Asp Lys His Leu Ile Ile Lys Pro Leu Ser Arg Arg Ala


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      100      105      110
Gly Val Asn Arg Lys Leu Asn Lys Asp Glu Ala His Asn Val Met Ser
      115      120      125
Asn Leu Tyr Tyr Pro Glu Val Arg Lys Ile Glu Asp Lys His Tyr Ile
      130      135      140
Glu Leu Phe Trp Asn Lys Val Tyr Tyr Phe Trp Ile Phe Phe Glu Phe
145      150      155      160
Ser Ile Ile Ala Leu Ile Ser Phe Leu Ile Ile Phe Phe Cys Lys Gln
      165      170      175
Met Asp Ile Phe His Val Glu Gly Ser Leu Leu Ser Leu Phe Phe Phe
      180      185      190
Val Ile Leu Ser Phe Ser Val Ser Gly Ile Ile Phe Ala Leu Thr Val
      195      200      205
Lys Pro Arg Thr Glu Ser Gln Val Gly Lys Ile Pro Asp Asp Lys Ile
210      215      220
Lys Glu Phe Phe Thr Lys Asn Asn Ile Asn
225      230

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<210> 351
 <211> 94
 <212> PRT
 <213> E. Coli

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      <400> 351
Met Phe Thr Ile Asn Ala Glu Val Arg Lys Glu Gln Gly Lys Gly Ala
 1      5      10      15
Ser Arg Arg Leu Arg Ala Ala Asn Lys Phe Pro Ala Ile Ile Tyr Gly
      20      25      30
Gly Lys Glu Ala Pro Leu Ala Ile Glu Leu Asp His Asp Lys Val Met
      35      40      45
Asn Met Gln Ala Lys Ala Glu Phe Tyr Ser Glu Val Leu Thr Ile Val
      50      55      60
Val Asp Gly Lys Glu Ile Lys Val Lys Ala Gln Asp Val Gln Arg His
65      70      75      80
Pro Tyr Lys Pro Lys Leu Gln His Ile Asp Phe Val Arg Ala
      85      90

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<210> 352
 <211> 658
 <212> PRT
 <213> E. Coli

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      <400> 352
Met Val Leu Phe Tyr Arg Ala His Trp Arg Asp Tyr Lys Asn Asp Gln
 1      5      10      15
Val Arg Ile Met Met Asn Leu Thr Thr Leu Thr His Arg Asp Ala Leu
      20      25      30
Cys Leu Asn Ala Arg Phe Thr Ser Arg Glu Glu Ala Ile His Ala Leu
      35      40      45
Thr Gln Arg Leu Ala Ala Leu Gly Lys Ile Ser Ser Thr Glu Gln Phe
      50      55      60
Leu Glu Glu Val Tyr Arg Arg Glu Ser Leu Gly Pro Thr Ala Leu Gly
65      70      75      80
Glu Gly Leu Ala Val Pro His Gly Lys Thr Ala Ala Val Lys Glu Ala
      85      90      95
Ala Phe Ala Val Ala Thr Leu Ser Glu Pro Leu Gln Trp Glu Gly Val
      100      105      110
Asp Gly Pro Glu Ala Val Asp Leu Val Val Leu Leu Ala Ile Pro Pro

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      115              120              125
Asn Glu Ala Gly Thr Thr His Met Gln Leu Leu Thr Ala Leu Thr Thr
  130              135              140
Arg Leu Ala Asp Asp Glu Ile Arg Ala Arg Ile Gln Ser Ala Thr Thr
  145              150              155              160
Pro Asp Glu Leu Leu Ser Ala Leu Asp Asp Lys Gly Gly Thr Gln Pro
      165              170              175
Ser Ala Ser Phe Ser Asn Ala Pro Thr Ile Val Cys Val Thr Ala Cys
      180              185              190
Pro Ala Gly Ile Ala His Thr Tyr Met Ala Ala Glu Tyr Leu Glu Lys
      195              200              205
Ala Gly Arg Lys Leu Gly Val Asn Val Tyr Val Glu Lys Gln Gly Ala
      210              215              220
Asn Gly Ile Glu Gly Arg Leu Thr Ala Asp Gln Leu Asn Ser Ala Thr
  225              230              235              240
Ala Cys Ile Phe Ala Ala Glu Val Ala Ile Lys Glu Ser Glu Arg Phe
      245              250              255
Asn Gly Ile Pro Ala Leu Ser Val Pro Val Ala Glu Pro Ile Arg His
      260              265              270
Ala Glu Ala Leu Ile Gln Gln Ala Leu Thr Leu Lys Arg Ser Asp Glu
      275              280              285
Thr Arg Thr Val Gln Gln Asp Thr Gln Pro Val Lys Ser Val Lys Thr
  290              295              300
Glu Leu Lys Gln Ala Leu Leu Ser Gly Ile Ser Phe Ala Val Pro Leu
  305              310              315              320
Ile Val Ala Gly Gly Thr Val Leu Ala Val Ala Val Leu Leu Ser Gln
      325              330              335
Ile Phe Gly Leu Gln Asp Leu Phe Asn Glu Glu Asn Ser Trp Leu Trp
      340              345              350
Met Tyr Arg Lys Leu Gly Gly Gly Leu Leu Gly Ile Leu Met Val Pro
      355              360              365
Val Leu Ala Ala Tyr Thr Ala Tyr Ser Leu Ala Asp Lys Pro Ala Leu
      370              375              380
Ala Pro Gly Phe Ala Ala Gly Leu Ala Ala Asn Met Ile Gly Ser Gly
  385              390              395              400
Phe Leu Gly Ala Val Val Gly Gly Leu Ile Ala Gly Tyr Leu Met Arg
      405              410              415
Trp Val Lys Asn His Leu Arg Leu Ser Ser Lys Phe Asn Gly Phe Leu
      420              425              430
Thr Phe Tyr Leu Tyr Pro Val Leu Gly Thr Leu Gly Ala Gly Ser Leu
      435              440              445
Met Leu Phe Val Val Gly Glu Pro Val Ala Trp Ile Asn Asn Ser Leu
      450              455              460
Thr Ala Trp Leu Asn Gly Leu Ser Gly Ser Asn Ala Leu Leu Leu Gly
  465              470              475              480
Ala Ile Leu Gly Phe Met Cys Ser Phe Asp Leu Gly Gly Pro Val Asn
      485              490              495
Lys Ala Ala Tyr Ala Phe Cys Leu Gly Ala Met Ala Asn Gly Val Tyr
      500              505              510
Gly Pro Tyr Ala Ile Phe Ala Ser Val Lys Met Val Ser Ala Phe Thr
      515              520              525
Val Thr Ala Ser Thr Met Leu Ala Pro Arg Leu Phe Lys Glu Phe Glu
      530              535              540
Ile Glu Thr Gly Lys Ser Thr Trp Leu Leu Gly Leu Ala Gly Ile Thr
  545              550              555              560
Glu Gly Ala Ile Pro Met Ala Ile Glu Asp Pro Leu Arg Val Ile Gly
      565              570              575
Ser Phe Val Leu Gly Ser Met Val Thr Gly Ala Ile Val Gly Ala Met
      580              585              590
Asn Ile Gly Leu Ser Thr Pro Gly Ala Gly Ile Phe Ser Leu Phe Leu
      595              600              605

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Leu His Asp Asn Gly Ala Gly Gly Val Met Ala Ala Ile Gly Trp Phe
 610 615 620
 Gly Ala Ala Leu Val Gly Ala Ala Ile Ser Thr Ala Ile Leu Leu Met
 625 630 635 640
 Trp Arg Arg His Ala Val Lys His Gly Asn Tyr Leu Thr Asp Gly Val
 645 650 655
 Met Pro

<210> 353
 <211> 877
 <212> PRT
 <213> E. Coli

<400> 353
 Met Lys Ala Val Ser Arg Val His Ile Thr Pro His Met His Trp Asp
 1 5 10 15
 Arg Glu Trp Tyr Phe Thr Thr Glu Glu Ser Arg Ile Leu Leu Val Asn
 20 25 30
 Asn Met Glu Glu Ile Leu Cys Arg Leu Glu Gln Asp Asn Glu Tyr Lys
 35 40 45
 Tyr Tyr Val Leu Asp Gly Gln Thr Ala Ile Leu Glu Asp Tyr Phe Ala
 50 55 60
 Val Lys Pro Glu Asn Lys Asp Arg Val Lys Lys Gln Val Glu Ala Gly
 65 70 75 80
 Lys Leu Ile Ile Gly Pro Trp Tyr Thr Gln Thr Asp Thr Thr Ile Val
 85 90 95
 Ser Ala Glu Ser Ile Val Arg Asn Leu Met Tyr Gly Met Arg Asp Cys
 100 105 110
 Leu Ala Phe Gly Glu Pro Met Lys Ile Gly Tyr Leu Pro Asp Ser Phe
 115 120 125
 Gly Met Ser Gly Gln Leu Pro His Ile Tyr Asn Gly Phe Gly Ile Thr
 130 135 140
 Arg Thr Met Phe Trp Arg Gly Cys Ser Glu Arg His Gly Thr Asp Lys
 145 150 155 160
 Thr Glu Phe Leu Trp Gln Ser Ser Asp Gly Ser Glu Val Thr Ala Gln
 165 170 175
 Val Leu Pro Leu Gly Tyr Ala Ile Gly Lys Tyr Leu Pro Ala Asp Glu
 180 185 190
 Asn Gly Leu Arg Lys Arg Leu Asp Ser Tyr Phe Asp Val Leu Glu Lys
 195 200 205
 Ala Ser Val Thr Lys Glu Ile Leu Leu Pro Asn Gly His Asp Gln Met
 210 215 220
 Pro Leu Gln Gln Asn Ile Phe Glu Val Met Asp Lys Leu Arg Glu Ile
 225 230 235 240
 Tyr Pro Gln Arg Lys Phe Val Met Ser Arg Phe Glu Glu Val Phe Glu
 245 250 255
 Lys Ile Glu Ala Gln Arg Asp Asn Leu Ala Thr Leu Lys Gly Glu Phe
 260 265 270
 Ile Asp Gly Lys Tyr Met Arg Val His Arg Thr Ile Gly Ser Thr Arg
 275 280 285
 Met Asp Ile Lys Ile Ala His Ala Arg Ile Glu Asn Lys Ile Val Asn
 290 295 300
 Leu Leu Glu Pro Leu Ala Thr Leu Ala Trp Thr Leu Gly Phe Glu Tyr
 305 310 315 320
 His His Gly Leu Leu Glu Lys Met Trp Lys Glu Ile Leu Lys Asn His
 325 330 335
 Ala His Asp Ser Ile Gly Cys Cys Cys Ser Asp Lys Val His Arg Glu
 340 345 350
 Ile Val Ala Arg Phe Glu Leu Ala Glu Asp Met Ala Asp Asn Leu Ile


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      355      360      365
Arg Phe Tyr Met Arg Lys Ile Ala Asp Asn Met Pro Gln Ser Asp Ala
370      375      380
Asp Lys Leu Val Leu Phe Asn Leu Met Pro Trp Pro Arg Glu Glu Val
385      390      400
Ile Asn Thr Thr Val Arg Leu Arg Ala Ser Gln Phe Asn Leu Arg Asp
405      410      415
Asp Arg Gly Gln Pro Val Pro Tyr Phe Ile Arg His Ala Arg Glu Ile
420      425      430
Asp Pro Gly Leu Ile Asp Arg Gln Ile Val His Tyr Gly Asn Tyr Asp
435      440      445
Pro Phe Met Glu Phe Asp Ile Gln Ile Asn Gln Ile Val Pro Ser Met
450      455      460
Gly Tyr Arg Thr Leu Tyr Ile Glu Ala Asn Gln Pro Gly Asn Val Ile
465      470      475
Ala Ala Lys Ser Asp Ala Glu Gly Ile Leu Glu Asn Ala Phe Trp Gln
485      490      495
Ile Ala Leu Asn Glu Asp Gly Ser Leu Gln Leu Val Asp Lys Asp Ser
500      505      510
Gly Val Arg Tyr Asp Arg Val Leu Gln Ile Glu Glu Ser Ser Asp Asp
515      520      525
Gly Asp Glu Tyr Asp Tyr Ser Pro Ala Lys Glu Glu Trp Val Ile Thr
530      535      540
Ala Ala Asn Ala Lys Pro Gln Cys Asp Ile Ile His Glu Ala Trp Gln
545      550      555
Ser Arg Ala Val Ile Arg Tyr Asp Met Ala Val Pro Leu Asn Leu Ser
565      570      575
Glu Arg Ser Ala Arg Gln Ser Thr Gly Arg Val Gly Val Val Leu Val
580      585      590
Val Thr Leu Ser His Asn Ser Arg Arg Ile Asp Val Asp Ile Asn Leu
595      600      605
Asp Asn Gln Ala Asp Asp His Arg Leu Arg Val Leu Val Pro Thr Pro
610      615      620
Phe Asn Thr Asp Ser Val Leu Ala Asp Thr Gln Phe Gly Ser Leu Thr
625      630      635
Arg Pro Val Asn Asp Ser Ala Met Asn Asn Trp Gln Gln Glu Gly Trp
645      650      655
Lys Glu Ala Pro Val Pro Val Trp Asn Met Leu Asn Tyr Val Ala Leu
660      665      670
Gln Glu Gly Arg Asn Gly Met Ala Val Phe Ser Glu Gly Leu Arg Glu
675      680      685
Phe Glu Val Ile Gly Glu Glu Lys Lys Thr Phe Ala Ile Thr Leu Leu
690      695      700
Arg Gly Val Gly Leu Leu Gly Lys Glu Asp Leu Leu Leu Arg Pro Gly
705      710      715
Arg Pro Ser Gly Ile Lys Met Pro Val Pro Asp Ser Gln Leu Arg Gly
725      730      735
Leu Leu Ser Cys Arg Leu Ser Leu Leu Ser Tyr Thr Gly Thr Pro Thr
740      745      750
Ala Ala Gly Val Ala Gln Gln Ala Arg Ala Trp Leu Thr Pro Val Gln
755      760      765
Cys Tyr Asn Lys Ile Pro Trp Asp Val Met Lys Leu Asn Lys Ala Gly
770      775      780
Phe Asn Val Pro Glu Ser Tyr Ser Leu Leu Lys Met Pro Pro Val Gly
785      790      795
Cys Leu Ile Ser Ala Leu Lys Lys Ala Glu Asp Arg Gln Glu Val Ile
805      810      815
Leu Arg Leu Phe Asn Pro Ala Glu Ser Ala Thr Cys Asp Ala Thr Val
820      825      830
Ala Phe Ser Arg Glu Val Ile Ser Cys Ser Glu Thr Met Met Asp Glu
835      840      845

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His Ile Thr Thr Glu Glu Asn Gln Gly Ser Asn Leu Ser Gly Pro Phe
 850 855 860
 Leu Pro Gly Gln Ser Arg Thr Phe Ser Tyr Arg Leu Ala
 865 870 875

<210> 354
 <211> 523
 <212> PRT
 <213> E. Coli

<400> 354
 Met Met Leu Asp Ile Val Glu Leu Ser Arg Leu Gln Phe Ala Leu Thr
 1 5 10 15
 Ala Met Tyr His Phe Leu Phe Val Pro Leu Thr Leu Gly Met Ala Phe
 20 25 30
 Leu Leu Ala Ile Met Glu Thr Val Tyr Val Leu Ser Gly Lys Gln Ile
 35 40 45
 Tyr Lys Asp Met Thr Lys Phe Trp Gly Lys Leu Phe Gly Ile Asn Phe
 50 55 60
 Ala Leu Gly Val Ala Thr Gly Leu Thr Met Glu Phe Gln Phe Gly Thr
 65 70 75 80
 Asn Trp Ser Tyr Tyr Ser His Tyr Val Gly Asp Ile Phe Gly Ala Pro
 85 90 95
 Leu Ala Ile Glu Gly Leu Met Ala Phe Phe Leu Glu Ser Thr Phe Val
 100 105 110
 Gly Leu Phe Phe Phe Gly Trp Asp Arg Leu Gly Lys Val Gln His Met
 115 120 125
 Cys Val Thr Trp Leu Val Ala Leu Gly Ser Asn Leu Ser Ala Leu Trp
 130 135 140
 Ile Leu Val Ala Asn Gly Trp Met Gln Asn Pro Ile Ala Ser Asp Phe
 145 150 155 160
 Asn Phe Glu Thr Met Arg Met Glu Met Val Ser Phe Ser Glu Leu Val
 165 170 175
 Leu Asn Pro Val Ala Gln Val Lys Phe Val His Thr Val Ala Ser Gly
 180 185 190
 Tyr Val Thr Gly Ala Met Phe Ile Leu Gly Ile Ser Ala Trp Tyr Met
 195 200 205
 Leu Lys Gly Arg Asp Phe Ala Phe Ala Lys Arg Ser Phe Ala Ile Ala
 210 215 220
 Ala Ser Phe Gly Met Ala Ala Val Leu Ser Val Ile Val Leu Gly Asp
 225 230 235 240
 Glu Ser Gly Tyr Glu Met Gly Asp Val Gln Lys Thr Lys Leu Ala Ala
 245 250 255
 Ile Glu Ala Glu Trp Glu Thr Gln Pro Ala Pro Ala Ala Phe Thr Leu
 260 265 270
 Phe Gly Ile Pro Asp Gln Glu Glu Glu Thr Asn Lys Phe Ala Ile Gln
 275 280 285
 Ile Pro Tyr Ala Leu Gly Ile Ile Ala Thr Arg Ser Val Asp Thr Pro
 290 295 300
 Val Ile Gly Leu Lys Glu Leu Met Val Gln His Glu Glu Arg Ile Arg
 305 310 315 320
 Asn Gly Met Lys Ala Tyr Ser Leu Leu Glu Gln Leu Arg Ser Gly Ser
 325 330 335
 Thr Asp Gln Ala Val Arg Asp Gln Phe Asn Ser Met Lys Lys Asp Leu
 340 345 350
 Gly Tyr Gly Leu Leu Leu Lys Arg Tyr Thr Pro Asn Val Ala Asp Ala
 355 360 365
 Thr Glu Ala Gln Ile Gln Gln Ala Thr Lys Asp Ser Ile Pro Arg Val
 370 375 380
 Ala Pro Leu Tyr Phe Ala Phe Arg Ile Met Val Ala Cys Gly Phe Leu


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385          390          395          400
Leu Leu Ala Ile Ile Ala Leu Ser Phe Trp Ser Val Ile Arg Asn Arg
          405          410          415
Ile Gly Glu Lys Lys Trp Leu Leu Arg Ala Ala Leu Tyr Gly Ile Pro
          420          425          430
Leu Pro Trp Trp Ile Ala Val Glu Ala Gly Trp Phe Val Ala Glu Tyr Gly
          435          440          445
Arg Gln Pro Trp Ala Ile Gly Glu Val Leu Pro Thr Ala Val Ala Asn
          450          455          460
Ser Ser Leu Thr Ala Gly Asp Leu Ile Phe Ser Met Val Leu Ile Cys
465          470          475          480
Gly Leu Tyr Thr Leu Phe Leu Val Ala Glu Leu Phe Leu Met Phe Lys
          485          490          495
Phe Ala Arg Leu Gly Pro Ser Ser Leu Lys Thr Gly Arg Tyr His Phe
          500          505          510
Glu Gln Ser Ser Thr Thr Thr Gln Pro Ala Arg
          515          520

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<210> 355
<211> 379
<212> PRT
<213> E. Coli

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<400> 355
Met Ile Asp Tyr Glu Val Leu Arg Phe Ile Trp Trp Leu Leu Val Gly
 1          5          10          15
Val Leu Leu Ile Gly Phe Ala Val Thr Asp Gly Phe Asp Met Gly Val
          20          25          30
Gly Met Leu Thr Arg Phe Leu Gly Arg Asn Asp Thr Glu Arg Arg Ile
          35          40          45
Met Ile Asn Ser Ile Ala Pro His Trp Asp Gly Asn Gln Val Trp Leu
50          55          60
Ile Thr Ala Gly Gly Ala Leu Phe Ala Ala Trp Pro Met Val Tyr Ala
65          70          75          80
Ala Ala Phe Ser Gly Phe Tyr Val Ala Met Ile Leu Val Leu Ala Ser
          85          90          95
Leu Phe Phe Arg Pro Val Gly Phe Asp Tyr Arg Ser Lys Ile Glu Glu
          100          105          110
Thr Arg Trp Arg Asn Met Trp Asp Trp Gly Ile Phe Ile Gly Ser Phe
          115          120          125
Val Pro Pro Leu Val Ile Gly Val Ala Phe Gly Asn Leu Leu Gln Gly
          130          135          140
Val Pro Phe Asn Val Asp Glu Tyr Leu Arg Leu Tyr Tyr Thr Gly Asn
145          150          155          160
Phe Phe Gln Leu Leu Asn Pro Phe Gly Leu Leu Ala Gly Val Val Ser
          165          170          175
Val Gly Met Ile Ile Thr Gln Gly Ala Thr Tyr Leu Gln Met Arg Thr
          180          185          190
Val Gly Glu Leu His Leu Arg Thr Arg Ala Thr Ala Gln Val Ala Ala
          195          200          205
Leu Val Thr Leu Val Cys Phe Ala Leu Ala Gly Val Trp Val Met Tyr
210          215          220
Gly Ile Asp Gly Tyr Val Val Lys Ser Thr Met Asp His Tyr Ala Ala
225          230          235          240
Ser Asn Pro Leu Asn Lys Glu Val Val Arg Glu Ala Gly Ala Trp Leu
          245          250          255
Val Asn Phe Asn Asn Thr Pro Ile Leu Trp Ala Ile Pro Ala Leu Gly
          260          265          270
Val Val Leu Pro Leu Leu Thr Ile Leu Thr Ala Arg Met Asp Lys Ala
          275          280          285

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Ala Trp Ala Phe Val Phe Ser Ser Leu Thr Leu Ala Cys Ile Ile Leu
 290 295 300
 Thr Ala Gly Ile Ala Met Phe Pro Phe Val Met Pro Ser Ser Thr Met
 305 310 315 320
 Met Asn Ala Ser Leu Thr Met Trp Asp Ala Thr Ser Ser Gln Leu Thr
 325 330 335
 Leu Asn Val Met Thr Trp Val Ala Val Val Leu Val Pro Ile Ile Leu
 340 345 350
 Leu Tyr Thr Ala Trp Cys Tyr Trp Lys Met Phe Gly Arg Ile Thr Lys
 355 360 365
 Glu Asp Ile Glu Arg Asn Thr His Ser Leu Tyr
 370 375

<210> 356

<211> 456

<212> PRT

<213> E. Coli

<400> 356

Met Glu Leu Ser Ser Leu Thr Ala Val Ser Pro Val Asp Gly Arg Tyr
 1 5 10 15
 Gly Asp Lys Val Ser Ala Leu Arg Gly Ile Phe Ser Glu Tyr Gly Leu
 20 25 30
 Leu Lys Phe Arg Val Gln Val Glu Val Arg Trp Leu Gln Lys Leu Ala
 35 40 45
 Ala His Ala Ala Ile Lys Glu Val Pro Ala Phe Ala Ala Asp Ala Ile
 50 55 60
 Gly Tyr Leu Asp Ala Ile Val Ala Ser Phe Ser Glu Glu Asp Ala Ala
 65 70 75 80
 Arg Ile Lys Thr Ile Glu Arg Thr Thr Asn His Asp Val Lys Ala Val
 85 90 95
 Glu Tyr Phe Leu Lys Glu Lys Val Ala Glu Ile Pro Glu Leu His Ala
 100 105 110
 Val Ser Glu Phe Ile His Phe Ala Cys Thr Ser Glu Asp Ile Asn Asn
 115 120 125
 Leu Ser His Ala Leu Met Leu Lys Thr Ala Arg Asp Glu Val Ile Leu
 130 135 140
 Pro Tyr Trp Arg Gln Leu Ile Asp Gly Ile Lys Asp Leu Ala Val Gln
 145 150 155 160
 Tyr Arg Asp Ile Pro Leu Leu Ser Arg Thr His Gly Gln Pro Ala Thr
 165 170 175
 Pro Ser Thr Ile Gly Lys Glu Met Ala Asn Val Ala Tyr Arg Met Glu
 180 185 190
 Arg Gln Tyr Arg Gln Leu Asn Gln Val Glu Ile Leu Gly Lys Ile Asn
 195 200 205
 Gly Ala Val Gly Asn Tyr Asn Ala His Ile Ala Ala Tyr Pro Glu Val
 210 215 220
 Asp Trp His Gln Phe Ser Glu Glu Phe Val Thr Ser Leu Gly Ile Gln
 225 230 235 240
 Trp Asn Pro Tyr Thr Gln Ile Glu Pro His Asp Tyr Ile Ala Glu
 245 250 255
 Leu Phe Asp Cys Val Ala Arg Phe Asn Thr Ile Leu Ile Asp Phe Asp
 260 265 270
 Arg Asp Val Trp Gly Tyr Ile Ala Leu Asn His Phe Lys Gln Lys Thr
 275 280 285
 Ile Ala Gly Glu Ile Gly Ser Ser Thr Met Pro His Lys Val Asn Pro
 290 295 300
 Ile Asp Phe Glu Asn Ser Glu Gly Asn Leu Gly Leu Ser Asn Ala Val
 305 310 315 320
 Leu Gln His Leu Ala Ser Lys Leu Pro Val Ser Arg Trp Gln Arg Asp


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          325          330          335
Leu Thr Asp Ser Thr Val Leu Arg Asn Leu Gly Val Gly Ile Gly Tyr
          340          345          350
Ala Leu Ile Ala Tyr Gln Ser Thr Leu Lys Gly Val Ser Lys Leu Glu
          355          360          365
Val Asn Arg Asp His Leu Leu Asp Glu Leu Asp His Asn Trp Glu Val
          370          375          380
Leu Ala Glu Pro Ile Gln Thr Val Met Arg Arg Tyr Gly Ile Glu Lys
          385          390          395          400
Pro Tyr Glu Lys Leu Lys Glu Leu Thr Arg Gly Lys Arg Val Asp Ala
          405          410          415
Glu Gly Met Lys Gln Phe Ile Asp Gly Leu Ala Leu Pro Glu Glu Glu
          420          425          430
Lys Ala Arg Leu Lys Ala Met Thr Pro Ala Asn Tyr Ile Gly Arg Ala
          435          440          445
Ile Thr Met Val Asp Glu Leu Lys
          450          455

```

<210> 357
 <211> 61
 <212> PRT
 <213> E. Coli

```

          <400> 357
Met Leu Ile Leu Thr Arg Arg Val Gly Glu Thr Leu Met Ile Gly Asp
  1          5          10          15
Glu Val Thr Val Thr Val Leu Gly Val Lys Gly Asn Gln Val Arg Ile
          20          25          30
Gly Val Asn Ala Pro Lys Glu Val Ser Val His Arg Glu Glu Ile Tyr
          35          40          45
Gln Arg Ile Gln Ala Glu Lys Ser Gln Gln Ser Ser Tyr
          50          55          60

```

<210> 358
 <211> 83
 <212> RNA
 <213> E. Coli

```

          <400> 358
ggugaggugg cccgagaggcu gaaggcgcuc cccugcuaag ggaguaugcg gucaaaagcu      60
gcauccgggg uucgaaucce cgccucaccg cca                                     83

```

<210> 359
 <211> 200
 <212> PRT
 <213> E. Coli

```

          <400> 359
Meu Lys Asn Lys Ala Asp Asn Lys Lys Arg Asn Phe Leu Thr His Ser
  1          5          10          15
Glu Ile Glu Ser Leu Leu Lys Ala Ala Asn Thr Gly Pro His Ala Ala
          20          25          30
Arg Asn Tyr Cys Leu Thr Leu Leu Cys Phe Ile His Gly Phe Arg Ala
          35          40          45
Ser Glu Ile Cys Arg Leu Arg Ile Ser Asp Ile Asp Leu Lys Ala Lys
          50          55          60
Cys Ile Tyr Ile His Arg Leu Lys Lys Gly Phe Ser Thr Thr His Pro
          65          70          75          80

```


Leu Leu Asn Lys Glu Val Gln Ala Leu Lys Asn Trp Leu Ser Ile Arg
 85 90 95
 Thr Ser Tyr Pro His Ala Glu Ser Glu Trp Val Phe Leu Ser Arg Lys
 100 105 110
 Gly Asn Pro Leu Ser Arg Gln Gln Phe Tyr His Ile Ile Ser Thr Ser
 115 120 125
 Gly Gly Asn Ala Gly Leu Ser Leu Glu Ile His Pro His Met Leu Arg
 130 135 140
 His Ser Cys Gly Phe Ala Leu Ala Asn Met Gly Ile Asp Thr Arg Leu
 145 150 155 160
 Ile Gln Asp Tyr Leu Gly His Arg Asn Ile Arg His Thr Val Trp Tyr
 165 170 175
 Thr Ala Ser Asn Ala Gly Arg Phe Tyr Gly Ile Trp Asp Arg Ala Arg
 180 185 190
 Gly Arg Gln Arg His Ala Val Leu
 195 200

<210> 360
 <211> 198
 <212> PRT
 <213> E. Coli

<400> 360
 Met Ser Lys Arg Arg Tyr Leu Thr Gly Lys Glu Val Gln Ala Met Met
 1 5 10 15
 Gln Ala Val Cys Tyr Gly Ala Thr Gly Ala Arg Asp Tyr Cys Leu Ile
 20 25 30
 Leu Leu Ala Tyr Arg His Gly Met Arg Ile Ser Glu Leu Leu Asp Leu
 35 40 45
 His Tyr Gln Asp Leu Asp Leu Asn Glu Gly Arg Ile Asn Ile Arg Arg
 50 55 60
 Leu Lys Asn Gly Phe Ser Thr Val His Pro Leu Arg Phe Asp Glu Arg
 65 70 75 80
 Glu Ala Val Glu Arg Trp Thr Gln Glu Arg Ala Asn Trp Lys Gly Ala
 85 90 95
 Asp Arg Thr Asp Ala Ile Phe Ile Ser Arg Arg Gly Ser Arg Leu Ser
 100 105 110
 Arg Gln Gln Ala Tyr Arg Ile Ile Arg Asp Ala Gly Ile Glu Ala Gly
 115 120 125
 Thr Val Thr Gln Thr His Pro His Met Leu Arg His Ala Cys Gly Tyr
 130 135 140
 Glu Leu Ala Glu Arg Gly Ala Asp Thr Arg Leu Ile Gln Asp Tyr Leu
 145 150 155 160
 Gly His Arg Asn Ile Arg His Thr Val Arg Tyr Thr Ala Ser Asn Ala
 165 170 175
 Ala Arg Phe Ala Gly Leu Trp Glu Arg Asn Asn Leu Ile Asn Glu Lys
 180 185 190
 Leu Lys Arg Glu Glu Val
 195

<210> 361
 <211> 182
 <212> PRT
 <213> E. Coli

<400> 361
 Met Lys Ile Lys Thr Leu Ala Ile Val Val Leu Ser Ala Leu Ser Leu
 1 5 10 15

Ser Ser Thr Ala Ala Leu Ala Ala Ala Thr Thr Val Asn Gly Gly Thr
 20 25 30
 Val His Phe Lys Gly Glu Val Val Asn Ala Ala Cys Ala Val Asp Ala
 35 40 45
 Gly Ser Val Asp Gln Thr Val Gln Leu Gly Gln Val Arg Thr Ala Ser
 50 55 60
 Leu Ala Gln Glu Gly Ala Thr Ser Ser Ala Val Gly Phe Asn Ile Gln
 65 70 75 80
 Leu Asn Asp Cys Asp Thr Asn Val Ala Ser Lys Ala Ala Val Ala Phe
 85 90 95
 Leu Gly Thr Ala Ile Asp Ala Gly His Thr Asn Val Leu Ala Leu Gln
 100 105 110
 Ser Ser Ala Ala Gly Ser Ala Thr Asn Val Gly Val Gln Ile Leu Asp
 115 120 125
 Arg Thr Gly Ala Ala Leu Thr Leu Asp Gly Ala Thr Phe Ser Ser Glu
 130 135 140
 Thr Thr Leu Asn Asn Gly Thr Asn Thr Ile Pro Phe Gln Ala Arg Tyr
 145 150 155 160
 Phe Ala Thr Gly Ala Ala Thr Pro Gly Ala Ala Asn Ala Asp Ala Thr
 165 170 175
 Phe Lys Val Gln Tyr Gln
 180

<210> 362
 <211> 215
 <212> PRT
 <213> E. Coli

<400> 362
 Met Leu Leu Met Arg Met Arg Pro Ser Arg Phe Ser Ile Asn Asn Leu
 1 5 10 15
 Pro Arg Phe Arg Asp Val Ile Thr Gly Arg Asp Ala His Pro Cys Ala
 20 25 30
 Ile Lys Ile Thr Met Lys Arg Lys Arg Leu Phe Leu Leu Ala Ser Leu
 35 40 45
 Leu Pro Met Phe Ala Leu Ala Gly Asn Lys Trp Asn Thr Thr Leu Pro
 50 55 60
 Gly Gly Asn Met Gln Phe Gln Gly Val Ile Ile Ala Glu Thr Cys Arg
 65 70 75 80
 Ile Glu Ala Gly Asp Lys Gln Met Thr Val Asn Met Gly Gln Ile Ser
 85 90 95
 Ser Asn Arg Phe His Ala Val Gly Glu Asp Ser Ala Pro Val Pro Phe
 100 105 110
 Val Ile His Leu Arg Glu Cys Ser Thr Val Val Ser Glu Arg Val Gly
 115 120 125
 Val Ala Phe His Gly Val Ala Asp Gly Lys Asn Pro Asp Val Leu Ser
 130 135 140
 Val Gly Glu Gly Pro Gly Ile Ala Thr Asn Ile Gly Val Ala Leu Phe
 145 150 155 160
 Asp Asp Glu Gly Asn Leu Val Pro Ile Asn Arg Pro Pro Ala Asn Trp
 165 170 175
 Lys Arg Leu Tyr Ser Gly Ser Thr Ser Leu His Phe Ile Ala Lys Tyr
 180 185 190
 Arg Ala Thr Gly Arg Arg Val Thr Gly Gly Ile Ala Asn Ala Gln Ala
 195 200 205
 Trp Phe Ser Leu Thr Tyr Gln
 210 215

<210> 363
 <211> 241
 <212> PRT
 <213> E. Coli

<400> 363

```

Met Ser Asn Lys Asn Val Asn Val Arg Lys Ser Gln Glu Ile Thr Phe
 1          5          10          15
Cys Leu Leu Ala Gly Ile Leu Met Phe Met Ala Met Met Val Ala Gly
 20          25          30
Arg Ala Glu Ala Gly Val Ala Leu Gly Ala Thr Arg Val Ile Tyr Pro
 35          40          45
Ala Gly Gln Lys Gln Glu Gln Leu Ala Val Thr Asn Asn Asp Glu Asn
 50          55          60
Ser Thr Tyr Leu Ile Gln Ser Trp Val Glu Asn Ala Asp Gly Val Lys
 65          70          75          80
Asp Gly Arg Phe Ile Val Thr Pro Pro Leu Phe Ala Met Lys Gly Lys
 85          90          95
Lys Glu Asn Thr Leu Arg Ile Leu Asp Ala Thr Asn Asn Gln Leu Pro
100          105          110
Gln Asp Arg Glu Ser Leu Phe Trp Met Asn Val Lys Ala Ile Pro Ser
115          120          125
Met Asp Lys Ser Lys Leu Thr Glu Asn Thr Leu Gln Leu Ala Ile Ile
130          135          140
Ser Arg Ile Lys Leu Tyr Tyr Arg Pro Ala Lys Leu Ala Leu Pro Pro
145          150          155          160
Asp Gln Ala Ala Glu Lys Leu Arg Phe Arg Arg Ser Ala Asn Ser Leu
165          170          175
Thr Leu Ile Asn Pro Thr Pro Tyr Tyr Leu Thr Val Thr Glu Leu Asn
180          185          190
Ala Gly Thr Arg Val Leu Glu Asn Ala Leu Val Pro Pro Met Gly Glu
195          200          205
Ser Thr Val Lys Leu Pro Ser Asp Ala Gly Ser Asn Ile Thr Tyr Arg
210          215          220
Thr Ile Asn Asp Tyr Gly Ala Leu Thr Pro Lys Met Thr Gly Val Met
225          230          235          240
Glu

```

<210> 364
 <211> 878
 <212> PRT
 <213> E. Coli

<400> 364

```

Met Ser Tyr Leu Asn Leu Arg Leu Tyr Gln Arg Asn Thr Gln Cys Leu
 1          5          10          15
His Ile Arg Lys His Arg Leu Ala Gly Phe Phe Val Arg Leu Val Val
 20          25          30
Ala Cys Ala Phe Ala Ala Gln Ala Pro Leu Ser Ser Ala Asp Leu Tyr
 35          40          45
Phe Asn Pro Arg Phe Leu Ala Asp Asp Pro Gln Ala Val Ala Asp Leu
 50          55          60
Ser Arg Phe Glu Asn Gly Gln Glu Leu Pro Pro Gly Thr Tyr Arg Val
 65          70          75          80
Asp Ile Tyr Leu Asn Asn Gly Tyr Met Ala Thr Arg Asp Val Thr Phe
 85          90          95
Asn Thr Gly Asp Ser Glu Gln Gly Ile Val Pro Cys Leu Thr Arg Ala
100          105          110
Gln Leu Ala Ser Met Gly Leu Asn Thr Ala Ser Val Ala Gly Met Asn

```


115	120	125
Leu Leu Ala Asp Asp Ala Cys Val Pro Leu Thr Thr Met Val Gln Asp		
130	135	140
Ala Thr Ala His Leu Asp Val Gly Gln Gln Arg Leu Asn Leu Thr Ile		
145	150	155
Pro Gln Ala Phe Met Ser Asn Arg Ala Arg Gly Tyr Ile Pro Pro Glu		
165	170	175
Leu Trp Asp Pro Gly Ile Asn Ala Gly Leu Leu Asn Tyr Asn Phe Ser		
180	185	190
Gly Asn Ser Val Gln Asn Arg Ile Gly Gly Asn Ser His Tyr Ala Tyr		
195	200	205
Leu Asn Leu Gln Ser Gly Leu Asn Ile Gly Ala Trp Arg Leu Arg Asp		
210	215	220
Asn Thr Thr Trp Ser Tyr Asn Ser Ser Asp Arg Ser Ser Gly Ser Lys		
225	230	235
Asn Lys Trp Gln His Ile Asn Thr Trp Leu Glu Arg Asp Ile Ile Pro		
245	250	255
Leu Arg Ser Arg Leu Thr Leu Gly Asp Gly Tyr Thr Gln Gly Asp Ile		
260	265	270
Phe Asp Gly Ile Asn Phe Arg Gly Ala Gln Leu Ala Ser Asp Asp Asn		
275	280	285
Met Leu Pro Asp Ser Gln Arg Gly Phe Ala Pro Val Ile His Gly Ile		
290	295	300
Ala Arg Gly Thr Ala Gln Val Thr Ile Lys Gln Asn Gly Tyr Asp Ile		
305	310	315
Tyr Asn Ser Thr Val Pro Pro Gly Pro Phe Thr Ile Asn Asp Ile Tyr		
325	330	335
Ala Ala Gly Asn Ser Gly Asp Leu Gln Val Thr Ile Lys Glu Ala Asp		
340	345	350
Gly Ser Thr Gln Ile Phe Thr Val Pro Tyr Ser Ser Val Pro Leu Leu		
355	360	365
Gln Arg Glu Gly His Thr Arg Tyr Ser Ile Thr Ala Gly Glu Tyr Arg		
370	375	380
Ser Gly Asn Ala Gln Gln Glu Lys Thr Arg Phe Phe Gln Ser Thr Leu		
385	390	395
Leu His Gly Leu Pro Ala Gly Trp Thr Ile Tyr Gly Gly Thr Gln Leu		
405	410	415
Ala Asp Arg Tyr Arg Ala Phe Asn Phe Gly Ile Gly Lys Asn Met Gly		
420	425	430
Ala Leu Gly Ala Leu Ser Val Asp Met Thr Gln Ala Asn Ser Thr Leu		
435	440	445
Pro Asp Asp Ser Gln His Asp Gly Gln Ser Val Arg Phe Leu Tyr Asn		
450	455	460
Lys Ser Leu Asn Glu Ser Gly Thr Asn Ile Gln Leu Val Gly Tyr Arg		
465	470	475
Tyr Ser Thr Ser Gly Tyr Phe Asn Phe Ala Asp Thr Thr Tyr Ser Arg		
485	490	495
Met Asn Gly Tyr Asn Ile Glu Thr Gln Asp Gly Val Ile Gln Val Lys		
500	505	510
Pro Lys Phe Thr Asp Tyr Tyr Asn Leu Ala Tyr Asn Lys Arg Gly Lys		
515	520	525
Leu Gln Leu Thr Val Thr Gln Gln Leu Gly Arg Thr Ser Thr Leu Tyr		
530	535	540
Leu Ser Gly Ser His Gln Thr Tyr Trp Gly Thr Ser Asn Val Asp Glu		
545	550	555
Gln Phe Gln Ala Gly Leu Asn Thr Ala Phe Glu Asp Ile Asn Trp Thr		
565	570	575
Leu Ser Tyr Ser Leu Thr Lys Asn Ala Trp Gln Lys Gly Arg Asp Gln		
580	585	590
Met Leu Ala Leu Asn Val Asn Ile Pro Phe Ser His Trp Leu Arg Ser		
595	600	605

Asp Ser Lys Ser Gln Trp Arg His Ala Ser Ala Ser Tyr Ser Met Ser
 610 615 620
 His Asp Leu Asn Gly Arg Met Thr Asn Leu Ala Gly Val Tyr Gly Thr
 625 630 635 640
 Leu Leu Glu Asp Asn Asn Leu Ser Tyr Ser Val Gln Thr Gly Tyr Ala
 645 650 655
 Gly Gly Gly Asp Gly Asn Ser Gly Ser Thr Gly Tyr Ala Thr Leu Asn
 660 665 670
 Tyr Arg Gly Gly Tyr Gly Asn Ala Asn Ile Gly Tyr Ser His Ser Asp
 675 680 685
 Asp Ile Lys Gln Leu Tyr Tyr Gly Val Ser Gly Gly Val Leu Ala His
 690 695 700
 Ala Asn Gly Val Thr Leu Gly Gln Pro Leu Asn Asp Thr Val Val Leu
 705 710 715 720
 Val Lys Ala Pro Gly Ala Lys Asp Ala Lys Val Glu Asn Gln Thr Gly
 725 730 735
 Val Arg Thr Asp Trp Arg Gly Tyr Ala Val Leu Pro Tyr Ala Thr Glu
 740 745 750
 Tyr Arg Glu Asn Arg Val Ala Leu Asp Thr Asn Thr Leu Ala Asp Asn
 755 760 765
 Val Asp Leu Asp Asn Ala Val Ala Asn Val Val Pro Thr Arg Gly Ala
 770 775 780
 Ile Val Arg Ala Glu Phe Lys Ala Arg Val Gly Ile Lys Leu Leu Met
 785 790 795 800
 Thr Leu Thr His Asn Asn Lys Pro Leu Pro Phe Gly Ala Met Val Thr
 805 810 815
 Ser Glu Ser Ser Gln Ser Ser Gly Ile Val Ala Asp Asn Gly Gln Val
 820 825 830
 Tyr Leu Ser Gly Met Pro Leu Ala Gly Lys Val Gln Val Lys Trp Gly
 835 840 845
 Glu Glu Glu Asn Ala His Cys Val Ala Asn Tyr Gln Leu Pro Pro Glu
 850 855 860
 Ser Gln Gln Gln Leu Leu Thr Gln Leu Ser Ala Glu Cys Arg
 865 870 875

<210> 365

<211> 176

<212> PRT

<213> E. Coli

<400> 365

Met Arg Asn Lys Pro Phe Tyr Leu Leu Cys Ala Phe Leu Trp Leu Ala
 1 5 10 15
 Val Ser His Ala Leu Ala Ala Asp Ser Thr Ile Thr Ile Arg Gly Tyr
 20 25 30
 Val Arg Asp Asn Gly Cys Ser Val Ala Ala Glu Ser Thr Asn Phe Thr
 35 40 45
 Val Asp Leu Met Glu Asn Ala Lys Gln Phe Asn Asn Ile Gly Ala
 50 55 60
 Thr Thr Pro Val Val Pro Phe Arg Ile Leu Leu Ser Pro Cys Gly Asn
 65 70 75 80
 Ala Val Ser Ala Val Lys Val Gly Phe Thr Gly Val Ala Asp Ser His
 85 90 95
 Asn Ala Asn Leu Leu Ala Leu Glu Asn Thr Val Ser Ala Ala Ser Gly
 100 105 110
 Leu Gly Ile Gln Leu Leu Asn Glu Gln Gln Asn Gln Ile Pro Leu Asn
 115 120 125
 Ala Pro Ser Ser Ala Leu Ser Trp Thr Thr Leu Thr Pro Gly Lys Pro
 130 135 140
 Asn Thr Leu Asn Phe Tyr Ala Arg Leu Met Ala Thr Gln Val Pro Val


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145              150              155              160
Thr Ala Gly His Ile Asn Ala Thr Ala Thr Phe Thr Leu Glu Tyr Gln
              165              170              175

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<210> 366
<211> 167
<212> PRT
<213> E. Coli
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	<400>	366													
Met 1	Lys	Trp	Cys 5	Lys	Arg	Gly	Tyr	Val	Leu 10	Ala	Ala	Ile	Leu	Ala 15	Leu
Ala	Ser	Ala	Thr 20	Ile	Gln	Ala	Ala	Asp 25	Val	Thr	Ile	Thr	Val 30	Asn	Gly
Lys	Val	Val 35	Ala	Lys	Pro	Cys	Thr 40	Val	Ser	Thr	Thr	Asn 45	Ala	Thr	Val
Asp 50	Leu	Gly	Asp	Leu	Tyr	Ser 55	Phe	Ser	Leu	Met	Ser 60	Ala	Gly	Ala	Ala
Ser 65	Ala	Trp	His	Asp 70	Val	Ala	Leu	Glu	Leu	Thr 75	Asn	Cys	Pro	Val	Gly 80
Thr	Ser	Arg	Val	Thr 85	Ala	Ser	Phe	Ser	Gly 90	Ala	Ala	Asp	Ser 95	Thr	Gly
Tyr	Tyr	Lys	Asn 100	Gln	Gly	Thr	Ala	Gln 105	Asn	Ile	Gln	Leu 110	Glu	Leu	Gln
Asp	Asp	Ser 115	Gly	Asn	Thr	Leu	Asn 120	Thr	Gly	Ala	Thr	Lys 125	Thr	Val	Gln
Val	Asp 130	Asp	Ser	Ser	Gln	Ser 135	Ala	His	Phe	Pro	Leu 140	Gln	Val	Arg	Ala
Leu 145	Thr	Val	Asn	Gly 150	Gly	Ala	Thr	Gln	Gly	Thr 155	Ile	Gln	Ala	Val	Ile 160
Ser	Ile	Thr	Tyr 165	Thr	Tyr	Ser									

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<210> 367
<211> 300
<212> PRT
<213> E. Coli
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<400> 367															
Met 1	Lys	Arg	Val	Ile 5	Thr	Leu	Phe	Ala	Val 10	Leu	Leu	Met	Gly	Trp 15	Ser
Val	Asn	Ala	Trp 20	Ser	Phe	Ala	Cys	Lys 25	Thr	Ala	Asn	Gly	Thr 30	Ala	Ile
Pro	Ile	Gly 35	Gly	Gly	Ser	Ala	Asn 40	Val	Tyr	Val	Asn	Leu 45	Ala	Pro	Val
Val 50	Asn	Val	Gly	Gln	Asn 55	Leu	Val	Val	Asp	Leu	Ser 60	Thr	Gln	Ile	Phe
Cys 65	His	Asn	Asp	Tyr 70	Pro	Glu	Thr	Ile	Thr 75	Asp	Tyr	Val	Thr	Leu 80	Gln
Arg	Gly	Ser	Ala 85	Tyr	Gly	Gly	Val	Leu	Ser 90	Asn	Phe	Ser	Gly 95	Thr	Val
Lys	Tyr	Ser	Gly 100	Ser	Ser	Tyr	Pro	Phe 105	Pro	Thr	Thr	Ser	Glu 110	Thr	Pro
Arg	Val	Val 115	Tyr	Asn	Ser	Arg	Thr 120	Asp	Lys	Pro	Trp	Pro 125	Val	Ala	Leu
Tyr	Leu 130	Thr	Pro	Val	Ser	Ser 135	Ala	Gly	Gly	Val	Ala 140	Ile	Lys	Ala	Gly

Ser Leu Ile Ala Val Leu Ile Leu Arg Gln Thr Asn Asn Tyr Asn Ser
 145 150 155 160
 Asp Asp Phe Gln Phe Val Trp Asn Ile Tyr Ala Asn Asn Asp Val Val
 165 170 175
 Val Pro Thr Gly Gly Cys Asp Val Ser Ala Arg Asp Val Thr Val Thr
 180 185 190
 Leu Pro Asp Tyr Pro Gly Ser Val Pro Ile Pro Leu Thr Val Tyr Cys
 195 200 205
 Ala Lys Ser Gln Asn Leu Gly Tyr Tyr Leu Ser Gly Thr Thr Ala Asp
 210 215 220
 Ala Gly Asn Ser Ile Phe Thr Asn Thr Ala Ser Phe Ser Pro Ala Gln
 225 230 235 240
 Gly Val Gly Val Gln Leu Thr Arg Asn Gly Thr Ile Ile Pro Ala Asn
 245 250 255
 Asn Thr Val Ser Leu Gly Ala Val Gly Thr Ser Ala Val Ser Leu Gly
 260 265 270
 Leu Thr Ala Asn Tyr Ala Arg Thr Gly Gly Gln Val Thr Ala Gly Asn
 275 280 285
 Val Gln Ser Ile Ile Gly Val Thr Phe Val Tyr Gln
 290 295 300

<210> 368
 <211> 521
 <212> PRT
 <213> E. Coli

<400> 368
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys
 1 5 10 15
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu
 20 25 30
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp
 35 40 45
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile
 50 55 60
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn
 65 70 75 80
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu
 85 90 95
 Ser Asn Asp Ser Arg Leu Thr Gly Cys Glu Arg Ser Pro Phe Glu Ser
 100 105 110
 Tyr Gly Asn Cys Ser Leu Thr Gly Gln Arg Thr Leu Arg Asn Phe Pro
 115 120 125
 Gly Cys Arg His Gly Pro Cys Arg Ser Cys Ala Gly Val Leu Gly Ser
 130 135 140
 Ser Gln Lys Glu Arg Pro Ala Ser Leu Pro Gly Ser Ser Arg Lys Ile
 145 150 155 160
 Val Arg Lys Ser Val Leu Ser Ala Ala Ser Val Leu Leu Asp Lys Ser
 165 170 175
 Cys Gln Ala Arg Ala Ser Ser Ser Ile Ser Met Asn Thr Lys Ile Arg
 180 185 190
 Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu Ile Gly Ala Gly Ala Ser
 195 200 205
 Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp Glu Lys Glu Gly Asn His
 210 215 220
 Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile Trp Thr Ile Cys Arg Gly
 225 230 235 240
 Ala Thr Val Val Asp Gly Lys Thr Val Phe Pro Asn Met Lys Leu Ser
 245 250 255

Lys Glu Lys Cys Asp Gln Val Asn Ala Ile Glu Arg Asp Lys Ala Leu
 260 265 270
 Ala Trp Val Glu Arg Asn Ile Lys Val Pro Leu Thr Glu Pro Gln Lys
 275 280 285
 Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn Ile Gly Pro Gly Lys Cys
 290 295 300
 Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn Ala Gly Asp Arg Lys Gly
 305 310 315 320
 Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys Asp Gly Gly Arg Asp Cys
 325 330 335
 Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln Val Ile Arg Arg Asp Gln
 340 345 350
 Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu Gln Ile Arg Tyr Ser Trp
 355 360 365
 Phe Phe Ser Cys Cys Gln Asp Leu Ser Ser Glu Met Ser Gly Ala Thr
 370 375 380
 Glu Asp Gly Lys Lys Asn Gly Arg Asn Val Met Leu Pro His Tyr His
 385 390 395 400
 Lys Arg Met Leu Asn Leu Leu Leu Glu Leu Asn Arg Gly Glu Leu Pro
 405 410 415
 Val Met Arg Leu Leu Lys Met Arg Asn Arg Asn Leu Leu Lys Phe Leu
 420 425 430
 Pro Gly Leu Leu Ile Cys Leu Ile Val Leu Thr Ser Cys Val Pro Lys
 435 440 445
 Gln Lys Asn Met Pro Tyr Ala Leu Thr Gln Arg Ser Ile Pro Gln Ile
 450 455 460
 Leu Pro Leu Pro Ser Glu Ala Lys Gln Pro Lys Pro Pro Lys Glu Cys
 465 470 475 480
 Ser Pro Thr Cys Ser Glu Ile Leu Gln Gln Lys Leu Ser Phe Met Leu
 485 490 495
 Lys Leu Leu Thr Asn Ala Thr Ser Gln Glu Leu Val Asn Arg Ser Met
 500 505 510
 Asn Leu Glu Ile Lys Ser Ile Lys Cys
 515 520

<210> 369
 <211> 177
 <212> PRT
 <213> E. Coli

<400> 369
 Met Asn Thr Lys Ile Arg Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu
 1 5 10 15
 Ile Gly Ala Gly Ala Ser Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp
 20 25 30
 Glu Lys Glu Gly Asn His Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile
 35 40 45
 Trp Thr Ile Cys Arg Gly Ala Thr Val Val Asp Gly Lys Thr Val Phe
 50 55 60
 Pro Asn Met Lys Leu Ser Lys Glu Lys Cys Asp Gln Val Asn Ala Ile
 65 70 75 80
 Glu Arg Asp Lys Ala Leu Ala Trp Val Glu Arg Asn Ile Lys Val Pro
 85 90 95
 Leu Thr Glu Pro Gln Lys Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn
 100 105 110
 Ile Gly Pro Gly Lys Cys Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn
 115 120 125
 Ala Gly Asp Arg Lys Gly Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys
 130 135 140

Asp Gly Gly Arg Asp Cys Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln
 145 150 155 160
 Val Ile Arg Arg Asp Gln Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu
 165 170 175
 Gln

<210> 370
 <211> 103
 <212> PRT
 <213> E. Coli

<400> 370
 Met Thr Gln Asp Tyr Glu Leu Val Val Lys Gly Val Arg Asn Phe Glu
 1 5 10 15
 Asn Lys Val Thr Val Thr Val Ala Leu Gln Asp Lys Glu Arg Phe Asp
 20 25 30
 Gly Glu Ile Phe Asp Leu Asp Val Ala Met Asp Arg Val Glu Gly Ala
 35 40 45
 Ala Leu Glu Phe Tyr Glu Ala Ala Ala Arg Arg Ser Val Arg Gln Val
 50 55 60
 Phe Leu Glu Val Ala Glu Lys Leu Ser Glu Lys Val Glu Ser Tyr Leu
 65 70 75 80
 Gln His Gln Tyr Ser Phe Lys Ile Glu Asn Pro Ala Asn Lys His Glu
 85 90 95
 Arg Pro His His Lys Tyr Leu
 100

<210> 371
 <211> 96
 <212> PRT
 <213> E. Coli

<400> 371
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys
 1 5 10 15
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu
 20 25 30
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp
 35 40 45
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile
 50 55 60
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn
 65 70 75 80
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu
 85 90 95

<210> 372
 <211> 71
 <212> PRT
 <213> E. Coli

<400> 372
 Met Ser Asn Lys Met Thr Gly Leu Val Lys Trp Phe Asn Ala Asp Lys
 1 5 10 15
 Gly Phe Gly Phe Ile Ser Pro Val Asp Gly Ser Lys Asp Val Phe Val

20 25 30
 His Phe Ser Ala Ile Gln Asn Asp Asn Tyr Arg Thr Leu Phe Glu Gly
 35 40 45
 Gln Lys Val Thr Phe Ser Ile Glu Ser Gly Ala Lys Gly Pro Ala Ala
 50 55 60
 Ala Asn Val Ile Ile Thr Asp
 65 70

<210> 373
 <211> 338
 <212> PRT
 <213> E. Coli

<400> 373
 Met Phe Val Ile Trp Ser His Arg Thr Gly Phe Ile Met Ser His Gln
 1 5 10 15
 Leu Thr Phe Ala Asp Ser Glu Phe Ser Lys Arg Arg Gln Thr Arg
 20 25 30
 Lys Glu Ile Phe Leu Ser Arg Met Glu Gln Ile Leu Pro Trp Gln Asn
 35 40 45
 Met Val Glu Val Ile Glu Pro Phe Tyr Pro Lys Ala Gly Asn Gly Arg
 50 55 60
 Arg Pro Tyr Pro Leu Glu Thr Met Leu Arg Ile His Cys Met Gln His
 65 70 75 80
 Trp Tyr Asn Leu Ser Asp Gly Ala Met Glu Asp Ala Leu Tyr Glu Ile
 85 90 95
 Ala Ser Met Arg Leu Phe Ala Arg Leu Ser Leu Asp Ser Ala Leu Pro
 100 105 110
 Asp Arg Thr Thr Ile Met Asn Phe Arg His Leu Leu Glu Gln His Gln
 115 120 125
 Leu Ala Arg Gln Leu Phe Lys Thr Ile Asn Arg Trp Leu Ala Glu Ala
 130 135 140
 Gly Val Met Met Thr Gln Gly Thr Leu Val Asp Ala Thr Ile Ile Glu
 145 150 155 160
 Ala Pro Ser Ser Thr Lys Asn Lys Glu Gln Gln Arg Asp Pro Glu Met
 165 170 175
 His Gln Thr Lys Lys Gly Asn Gln Trp His Phe Gly Met Lys Ala His
 180 185 190
 Ile Gly Val Asp Ala Lys Ser Gly Leu Thr His Ser Leu Val Thr Thr
 195 200 205
 Ala Ala Asn Glu His Asp Leu Asn Gln Leu Gly Asn Leu Leu His Gly
 210 215 220
 Glu Glu Gln Phe Val Ser Ala Asp Ala Gly Tyr Gln Gly Ala Pro Gln
 225 230 235 240
 Arg Glu Glu Leu Ala Glu Val Asp Val Asp Trp Leu Ile Ala Glu Arg
 245 250 255
 Pro Gly Lys Val Arg Thr Leu Lys Gln His Pro Arg Lys Asn Lys Thr
 260 265 270
 Ala Ile Asn Ile Glu Tyr Met Lys Ala Ser Ile Arg Ala Arg Val Glu
 275 280 285
 His Pro Phe Arg Ile Ile Lys Arg Gln Phe Gly Phe Val Lys Ala Arg
 290 295 300
 Tyr Lys Gly Leu Leu Lys Asn Asp Asn Gln Leu Ala Met Leu Phe Thr
 305 310 315 320
 Leu Ala Asn Leu Phe Arg Ala Asp Gln Met Ile Arg Gln Trp Glu Arg
 325 330 335
 Ser His

<210> 374
 <211> 157
 <212> PRT
 <213> E. Coli

<400> 374
 Met Val Tyr Ile Ile Val Ser His Gly His Glu Asp Tyr Ile Lys
 1 5 10 15
 Lys Leu Leu Glu Asn Leu Asn Ala Asp Asp Glu His Tyr Lys Ile Ile
 20 25 30
 Val Arg Asp Asn Lys Asp Ser Leu Leu Leu Lys Gln Ile Cys Gln His
 35 40 45
 Tyr Ala Gly Leu Asp Tyr Ile Ser Gly Gly Val Tyr Gly Phe Gly His
 50 55 60
 Asn Asn Asn Ile Ala Val Ala Tyr Val Lys Glu Lys Tyr Arg Pro Ala
 65 70 75 80
 Asp Asp Asp Tyr Ile Leu Phe Leu Asn Pro Asp Ile Ile Met Lys His
 85 90 95
 Asp Asp Leu Leu Thr Tyr Ile Lys Tyr Val Glu Ser Lys Arg Tyr Ala
 100 105 110
 Phe Ser Thr Leu Cys Leu Phe Arg Asp Glu Ala Lys Ser Leu His Asp
 115 120 125
 Tyr Ser Val Arg Lys Phe Pro Val Leu Ser Asp Phe Ile Val Ser Phe
 130 135 140
 Met Leu Gly Ile Lys Glu Gly Ala Asn Lys Ser Leu Ile
 145 150 155

<210> 375
 <211> 372
 <212> PRT
 <213> E. Coli

<400> 375
 Met Gly Lys Ser Ile Val Val Val Ser Ala Val Asn Phe Thr Thr Gly
 1 5 10 15
 Gly Pro Phe Thr Ile Leu Lys Lys Phe Leu Ala Ala Thr Asn Asn Lys
 20 25 30
 Glu Asn Val Ser Phe Ile Ala Leu Val His Ser Ala Lys Glu Leu Lys
 35 40 45
 Glu Ser Tyr Pro Trp Val Lys Phe Ile Glu Phe Pro Glu Val Lys Gly
 50 55 60
 Ser Trp Leu Lys Arg Leu His Phe Glu Tyr Val Val Cys Lys Lys Leu
 65 70 75 80
 Ser Lys Glu Leu Asn Ala Thr His Trp Ile Cys Leu His Asp Ile Thr
 85 90 95
 Ala Asn Val Val Thr Lys Lys Arg Tyr Val Tyr Cys His Asn Pro Ala
 100 105 110
 Pro Phe Tyr Lys Gly Ile Leu Phe Arg Glu Ile Leu Met Glu Pro Ser
 115 120 125
 Phe Phe Leu Phe Lys Met Leu Tyr Gly Leu Ile Tyr Lys Ile Asn Ile
 130 135 140
 Lys Lys Asn Thr Ala Val Phe Val Gln Gln Phe Trp Met Lys Glu Lys
 145 150 155 160
 Phe Ile Lys Lys Tyr Ser Ile Asn Asn Ile Ile Val Ser Arg Pro Glu
 165 170 175
 Ile Lys Leu Ser Asp Lys Ser Gln Leu Thr Asp Asp Asp Ser Gln Phe
 180 185 190
 Lys Asn Asn Pro Ser Glu Leu Thr Ile Phe Tyr Pro Ala Val Pro Arg

195 200 205
 Val Phe Lys Asn Tyr Glu Leu Ile Ile Ser Ala Ala Arg Lys Leu Lys
 210 215 220
 Glu Gln Ser Asn Ile Lys Phe Leu Leu Thr Ile Ser Gly Thr Glu Asn
 225 230 235 240
 Ala Tyr Ala Lys Tyr Ile Ile Ser Leu Ala Glu Gly Leu Asp Asn Val
 245 250 255
 His Phe Leu Gly Tyr Leu Asp Lys Glu Lys Ile Asp His Cys Tyr Asn
 260 265 270
 Ile Ser Asp Ile Val Cys Phe Pro Ser Arg Leu Glu Thr Trp Gly Leu
 275 280 285
 Pro Leu Ser Glu Ala Lys Glu Arg Gly Lys Trp Val Leu Ala Ser Asp
 290 295 300
 Phe Pro Phe Thr Arg Glu Thr Leu Gly Ser Tyr Glu Lys Lys Ala Phe
 305 310 315 320
 Phe Asp Ser Asn Asn Asp Asp Met Leu Val Lys Leu Ile Ile Asp Phe
 325 330 335
 Lys Lys Gly Asn Leu Lys Lys Asp Ile Ser Asp Ala Asn Phe Ile Tyr
 340 345 350
 Arg Asn Glu Asn Val Leu Val Gly Phe Asp Glu Leu Val Asn Phe Ile
 355 360 365
 Thr Glu Glu His
 370

<210> 376
 <211> 196
 <212> PRT
 <213> E. Coli

<400> 376
 Met Ile Leu Lys Leu Ala Lys Arg Tyr Gly Leu Cys Gly Phe Ile Arg
 1 5 10 15
 Leu Val Arg Asp Val Leu Leu Thr Arg Val Phe Tyr Arg Asn Cys Arg
 20 25 30
 Ile Ile Arg Phe Pro Cys Tyr Ile Arg Asn Asp Gly Ser Ile Asn Phe
 35 40 45
 Gly Glu Asn Phe Thr Ser Gly Val Gly Leu Arg Leu Asp Ala Phe Gly
 50 55 60
 Arg Gly Val Ile Phe Phe Ser Asp Asn Val Gln Val Asn Asp Tyr Val
 65 70 75 80
 His Ile Ala Ser Ile Glu Ser Val Thr Ile Gly Arg Asp Thr Leu Ile
 85 90 95
 Ala Ser Lys Val Phe Ile Thr Asp His Asn His Gly Ser Phe Lys His
 100 105 110
 Ser Asp Pro Met Ser Ser Pro Asn Ile Pro Pro Asp Met Arg Thr Leu
 115 120 125
 Glu Ser Ser Ala Val Val Ile Gly Gln Arg Val Trp Leu Gly Glu Asn
 130 135 140
 Val Thr Val Leu Pro Gly Thr Ile Ile Gly Asn Gly Val Val Val Gly
 145 150 155 160
 Ala Asn Ser Val Val Arg Gly Ser Ile Pro Glu Asn Thr Val Ile Ala
 165 170 175
 Gly Val Pro Ala Lys Ile Ile Lys Lys Tyr Asn His Glu Thr Lys Leu
 180 185 190
 Trp Glu Lys Ala
 195

<210> 377
 <211> 330
 <212> PRT

<213> E. Coli

<400> 377

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Met Tyr Phe Leu Asn Asp Leu Asn Phe Ser Arg Arg Asp Ala Gly Phe
1      5      10      15
Lys Ala Arg Lys Asp Ala Leu Asp Ile Ala Ser Asp Tyr Glu Asn Ile
20      25      30
Ser Val Val Asn Ile Pro Leu Trp Gly Gly Val Val Gln Arg Ile Ile
35      40      45
Ser Ser Val Lys Leu Ser Thr Phe Leu Cys Gly Leu Glu Asn Lys Asp
50      55      60
Val Leu Ile Phe Asn Phe Pro Met Ala Lys Pro Phe Trp His Ile Leu
65      70      75      80
Ser Phe Phe His Arg Leu Leu Lys Phe Arg Ile Val Pro Leu Ile His
85      90      95
Asp Ile Asp Glu Leu Arg Gly Gly Gly Gly Ser Asp Ser Val Arg Leu
100     105     110
Ala Thr Cys Asp Met Val Ile Ser His Asn Pro Gln Met Thr Lys Tyr
115     120     125
Leu Ser Lys Tyr Met Ser Gln Asp Lys Ile Lys Asp Ile Lys Ile Phe
130     135     140
Asp Tyr Leu Val Ser Ser Asp Val Glu His Arg Asp Val Thr Asp Lys
145     150     155     160
Gln Arg Gly Val Ile Tyr Ala Gly Asn Leu Ser Arg His Lys Cys Ser
165     170     175
Phe Ile Tyr Thr Glu Gly Cys Asp Phe Thr Leu Phe Gly Val Asn Tyr
180     185     190
Glu Asn Lys Asp Asn Pro Lys Tyr Leu Gly Ser Phe Asp Ala Gln Ser
195     200     205
Pro Glu Lys Ile Asn Leu Pro Gly Met Gln Phe Gly Leu Ile Trp Asp
210     215     220
Gly Asp Ser Val Glu Thr Cys Ser Gly Ala Phe Gly Asp Tyr Leu Lys
225     230     235     240
Phe Asn Asn Pro His Lys Thr Ser Leu Tyr Leu Ser Met Glu Leu Pro
245     250     255
Val Phe Ile Trp Asp Lys Ala Ala Leu Ala Asp Phe Ile Val Asp Asn
260     265     270
Arg Ile Gly Tyr Ala Val Gly Ser Ile Lys Glu Met Gln Glu Ile Val
275     280     285
Asp Ser Met Thr Ile Glu Thr Tyr Lys Gln Ile Ser Glu Asn Thr Lys
290     295     300
Ile Ile Ser Gln Lys Ile Arg Thr Gly Ser Tyr Phe Arg Asp Val Leu
305     310     315     320
Glu Glu Val Ile Asp Asp Leu Lys Thr Arg
325     330

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<210> 378

<211> 388

<212> PRT

<213> E. Coli

<400> 378

```

Met Ile Tyr Leu Val Ile Ser Val Phe Leu Ile Thr Ala Phe Ile Cys
1      5      10      15
Leu Tyr Leu Lys Lys Asp Ile Phe Tyr Pro Ala Val Cys Val Asn Ile
20      25      30
Ile Phe Ala Leu Val Leu Leu Gly Tyr Glu Ile Thr Ser Asp Ile Tyr
35      40      45
Ala Phe Gln Leu Asn Asp Ala Thr Leu Ile Phe Leu Leu Cys Asn Val
50      55      60

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Leu Thr Phe Thr Leu Ser Cys Leu Leu Thr Glu Ser Val Leu Asp Leu
 65 70 75 80
 Asn Ile Arg Lys Val Asn Asn Ala Ile Tyr Ser Ile Pro Ser Lys Lys
 85 90 95
 Val His Asn Val Gly Leu Leu Val Ile Ser Phe Ser Met Ile Tyr Ile
 100 105 110
 Cys Met Arg Leu Ser Asn Tyr Gln Phe Gly Thr Ser Leu Leu Ser Tyr
 115 120 125
 Met Asn Leu Ile Arg Asp Ala Asp Val Glu Asp Thr Ser Arg Asn Phe
 130 135 140
 Ser Ala Tyr Met Gln Pro Ile Ile Leu Thr Thr Phe Ala Leu Phe Ile
 145 150 155 160
 Trp Ser Lys Lys Phe Thr Asn Thr Lys Val Ser Lys Thr Phe Thr Leu
 165 170 175
 Leu Val Phe Ile Val Phe Ile Phe Ala Ile Ile Leu Asn Thr Gly Lys
 180 185 190
 Gln Ile Val Phe Met Val Ile Ile Ser Tyr Ala Phe Ile Val Gly Val
 195 200 205
 Asn Arg Val Lys His Tyr Val Tyr Leu Ile Thr Ala Val Gly Val Leu
 210 215 220
 Phe Ser Leu Tyr Met Leu Phe Leu Arg Gly Leu Pro Gly Gly Met Ala
 225 230 235 240
 Tyr Tyr Leu Ser Met Tyr Leu Val Ser Pro Ile Ile Ala Phe Gln Glu
 245 250 255
 Phe Tyr Phe Gln Gln Val Ser Asn Ser Ala Ser Ser His Val Phe Trp
 260 265 270
 Phe Phe Glu Arg Leu Met Gly Leu Leu Thr Gly Gly Val Ser Met Ser
 275 280 285
 Leu His Lys Glu Phe Val Trp Val Gly Leu Pro Thr Asn Val Tyr Thr
 290 295 300
 Ala Phe Ser Asp Tyr Val Tyr Ile Ser Ala Glu Leu Ser Tyr Leu Met
 305 310 315 320
 Met Val Ile His Gly Cys Ile Ser Gly Val Leu Trp Arg Leu Ser Arg
 325 330 335
 Asn Tyr Ile Ser Val Lys Ile Phe Tyr Ser Tyr Phe Ile Tyr Thr Phe
 340 345 350
 Ser Phe Ile Phe Tyr His Glu Ser Phe Met Thr Asn Ile Ser Ser Trp
 355 360 365
 Ile Gln Ile Thr Leu Cys Ile Ile Val Phe Ser Gln Phe Leu Lys Ala
 370 375 380
 Gln Lys Ile Lys
 385

<210> 379

<211> 367

<212> PRT

<213> E. Coli

<400> 379

Met Tyr Asp Tyr Ile Ile Val Gly Ser Gly Leu Phe Gly Ala Val Cys
 1 5 10 15
 Ala Asn Glu Leu Lys Lys Leu Asn Lys Lys Val Leu Val Ile Glu Lys
 20 25 30
 Arg Asn His Ile Gly Gly Asn Ala Tyr Thr Glu Asp Cys Glu Gly Ile
 35 40 45
 Gln Ile His Lys Tyr Gly Ala His Ile Phe His Thr Asn Asp Lys Tyr
 50 55 60
 Ile Trp Asp Tyr Val Asn Asp Leu Val Glu Phe Asn Arg Phe Thr Asn
 65 70 75 80

Ser	Pro	Leu	Ala	Ile	Tyr	Lys	Asp	Lys	Leu	Phe	Asn	Leu	Pro	Phe	Asn
Met	Asn	Thr	Phe	His	Gln	Met	Trp	Gly	Val	Lys	Asp	Pro	Gln	Glu	Ala
Gln	Asn	Ile	Ile	Asn	Ala	Gln	Lys	Lys	Lys	Tyr	Gly	Asp	Lys	Val	Pro
Glu	Asn	Leu	Glu	Glu	Gln	Ala	Ile	Ser	Leu	Val	Gly	Glu	Asp	Leu	Tyr
Gln	Ala	Leu	Ile	Lys	Gly	Tyr	Thr	Glu	Lys	Gln	Trp	Gly	Arg	Ser	Ala
Lys	Glu	Leu	Pro	Ala	Phe	Ile	Ile	Lys	Arg	Ile	Pro	Val	Arg	Phe	Thr
Phe	Asp	Asn	Asn	Tyr	Phe	Ser	Asp	Arg	Tyr	Gln	Gly	Ile	Pro	Val	Gly
Gly	Tyr	Thr	Lys	Leu	Ile	Glu	Lys	Met	Leu	Glu	Gly	Val	Asp	Val	Lys
Leu	Gly	Ile	Asp	Phe	Leu	Lys	Asp	Lys	Asp	Ser	Leu	Ala	Ser	Lys	Ala
His	Arg	Ile	Ile	Tyr	Thr	Gly	Pro	Ile	Asp	Gln	Tyr	Phe	Asp	Tyr	Arg
Phe	Gly	Ala	Leu	Glu	Tyr	Arg	Ser	Leu	Lys	Phe	Glu	Thr	Glu	Arg	His
Glu	Phe	Pro	Asn	Phe	Gln	Gly	Asn	Ala	Val	Ile	Asn	Phe	Thr	Asp	Ala
Asn	Val	Pro	Tyr	Thr	Arg	Ile	Ile	Glu	His	Lys	His	Phe	Asp	Tyr	Val
Glu	Thr	Lys	His	Thr	Val	Val	Thr	Lys	Glu	Tyr	Pro	Leu	Glu	Trp	Lys
Val	Gly	Asp	Glu	Pro	Tyr	Tyr	Pro	Val	Asn	Asp	Asn	Lys	Asn	Met	Glu
Leu	Phe	Lys	Lys	Tyr	Arg	Glu	Leu	Ala	Ser	Arg	Glu	Asp	Lys	Val	Ile
Phe	Gly	Gly	Arg	Leu	Ala	Glu	Tyr	Lys	Tyr	Tyr	Asp	Met	His	Gln	Val
Ile	Ser	Ala	Ala	Leu	Tyr	Gln	Val	Lys	Asn	Ile	Met	Ser	Thr	Asp	

<210> 380

<211> 371

<212> PRT

<213> E. Coli

<400> 380

Met 1	Phe	Pro	Lys	Ile 5	Met	Asn	Asp	Glu	Asn 10	Phe	Phe	Lys	Lys	Ala 15	Ala
Ala	His	Gly	Glu 20	Glu	Pro	Pro	Leu	Thr 25	Pro	Gln	Asn	Glu	His 30	Gln	Arg
Ser	Gly	Leu 35	Arg	Phe	Ala	Arg	Arg 40	Val	Arg	Leu	Pro	Arg 45	Ala	Val	Gly
Leu 50	Ala	Gly	Met	Phe	Leu	Pro 55	Ile	Ala	Ser	Thr	Leu 60	Val	Ser	His	Pro
Pro 65	Pro	Gly	Trp	Trp	Trp 70	Leu	Val	Leu	Val	Gly 75	Trp	Ala	Phe	Val	Trp 80
Pro	His	Leu	Ala 85	Trp	Gln	Ile	Ala	Ser 90	Arg	Ala	Val	Asp	Pro 95	Leu	Ser
Arg	Glu	Ile 100	Tyr	Asn	Leu	Lys	Thr	Asp 105	Ala	Val	Leu	Ala 110	Gly	Met	Trp
Val	Gly	Val 115	Met	Gly	Val	Asn 120	Val	Leu	Pro	Ser	Thr 125	Ala	Met	Leu	Met
Ile	Met	Cys	Leu	Asn	Leu	Met	Gly	Ala	Gly	Gly	Pro	Arg	Leu	Phe	Val

130 135 140
 Ala Gly Leu Val Leu Met Val Val Ser Cys Leu Val Thr Leu Glu Leu
 145 150 155 160
 Thr Gly Ile Thr Val Ser Phe Asn Ser Ala Pro Leu Glu Trp Trp Leu
 165 170 175
 Ser Leu Pro Ile Ile Val Ile Tyr Pro Leu Leu Phe Gly Trp Val Ser
 180 185 190
 Tyr Gln Thr Ala Thr Lys Leu Ala Glu His Lys Arg Arg Leu Gln Val
 195 200 205
 Met Ser Thr Arg Asp Gly Met Thr Gly Val Tyr Asn Arg Arg His Trp
 210 215 220
 Glu Thr Met Leu Arg Asn Glu Phe Asp Asn Cys Arg Arg His Asn Arg
 225 230 235 240
 Asp Ala Thr Leu Leu Ile Ile Asp Ile Asp His Phe Lys Ser Ile Asn
 245 250 255
 Asp Thr Trp Gly His Asp Val Gly Asp Glu Ala Ile Val Ala Leu Thr
 260 265 270
 Arg Gln Leu Gln Ile Thr Leu Arg Gly Ser Asp Val Ile Gly Arg Phe
 275 280 285
 Gly Gly Asp Glu Phe Ala Val Ile Met Ser Gly Thr Pro Ala Glu Ser
 290 295 300
 Ala Ile Thr Ala Met Leu Arg Val His Glu Gly Leu Asn Thr Leu Arg
 305 310 315 320
 Leu Pro Asn Thr Pro Gln Val Thr Leu Arg Ile Ser Val Gly Val Ala
 325 330 335
 Pro Leu Asn Pro Gln Met Ser His Tyr Arg Glu Trp Leu Lys Ser Ala
 340 345 350
 Asp Leu Ala Leu Tyr Lys Ala Lys Lys Ala Gly Arg Asn Arg Thr Glu
 355 360 365
 Val Ala Ala
 370

<210> 381

<211> 467

<212> PRT

<213> E. Coli

<400> 381

Met Asp Val Asn Val Asp Gln Phe Asp Thr Glu Ala Phe Arg Thr Asp
 1 5 10 15
 Lys Leu Glu Leu Thr Ser Gly Asn Ile Ala Asp His Asn Gly Asn Val
 20 25 30
 Val Ser Gly Val Phe Asp Ile His Ser Ser Asp Tyr Val Leu Asn Ala
 35 40 45
 Asp Leu Val Asn Asp Arg Thr Trp Asp Thr Ser Lys Ser Asn Tyr Gly
 50 55 60
 Tyr Gly Ile Val Ala Met Asn Ser Asp Gly His Leu Thr Ile Asn Gly
 65 70 75 80
 Asn Gly Asp Val Asp Asn Gly Thr Glu Leu Asp Asn Ser Ser Val Asp
 85 90 95
 Asn Val Val Ala Ala Thr Gly Asn Tyr Lys Val Arg Ile Asp Asn Ala
 100 105 110
 Thr Gly Ala Gly Ala Ile Ala Asp Tyr Lys Asp Lys Glu Ile Ile Tyr
 115 120 125
 Val Asn Asp Val Asn Ser Asn Ala Thr Phe Ser Ala Ala Asn Lys Ala
 130 135 140
 Asp Leu Gly Ala Tyr Thr Gln Ala Glu Gln Arg Gly Asn Thr Val
 145 150 155 160
 Val Leu Gln Gln Met Glu Leu Thr Asp Tyr Ala Asn Met Ala Leu Ser
 165 170 175
 Ile Pro Ser Ala Asn Thr Asn Ile Trp Asn Leu Glu Gln Asp Thr Val


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      180      185      190
Gly Thr Arg Leu Thr Asn Ser Arg His Gly Leu Ala Asp Asn Gly Gly
      195      200      205
Ala Trp Val Ser Tyr Phe Gly Gly Asn Phe Asn Gly Asp Asn Gly Thr
      210      215      220
Ile Asn Tyr Asp Gln Asp Val Asn Gly Ile Met Val Gly Val Asp Thr
      225      230      235      240
Lys Ile Asp Gly Asn Asn Ala Lys Trp Ile Val Gly Ala Ala Ala Gly
      245      250      255
Phe Ala Lys Gly Asp Met Asn Asp Arg Ser Gly Gln Val Asp Gln Asp
      260      265      270
Ser Gln Thr Ala Tyr Ile Tyr Ser Ser Ala His Phe Ala Asn Asn Val
      275      280      285
Phe Val Asp Gly Ser Leu Ser Tyr Ser His Phe Asn Asn Asp Leu Ser
      290      295      300
Ala Thr Met Ser Asn Gly Thr Tyr Val Asp Gly Ser Thr Asn Ser Asp
      305      310      315      320
Ala Trp Gly Phe Gly Leu Lys Ala Gly Tyr Asp Phe Lys Leu Gly Asp
      325      330      335
Ala Gly Tyr Val Thr Pro Tyr Gly Ser Val Ser Gly Leu Phe Gln Ser
      340      345      350
Gly Asp Asp Tyr Gln Leu Ser Asn Asp Met Lys Val Asp Gly Gln Ser
      355      360      365
Tyr Asp Ser Met Arg Tyr Glu Leu Gly Val Asp Ala Gly Tyr Thr Phe
      370      375      380
Thr Tyr Ser Glu Asp Gln Ala Leu Thr Pro Tyr Phe Lys Leu Ala Tyr
      385      390      395      400
Val Tyr Asp Asp Ser Asn Asn Asp Asn Asp Val Asn Gly Asp Ser Ile
      405      410      415
Asp Asn Gly Thr Glu Gly Ser Ala Val Arg Val Gly Leu Gly Thr Gln
      420      425      430
Phe Ser Phe Thr Lys Asn Phe Ser Ala Tyr Thr Asp Ala Asn Tyr Leu
      435      440      445
Gly Gly Gly Asp Val Asp Gln Asp Trp Ser Ala Asn Val Gly Val Lys
      450      455      460
Tyr Thr Trp
465

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<210> 382
 <211> 222
 <212> PRT
 <213> E. Coli

```

      <400> 382
Met Pro Val Lys Asp Leu Thr Gly Ile Thr Ala Lys Asp Ala Gln Met
      1      5      10      15
Leu Ser Val Val Lys Pro Leu Gln Glu Phe Gly Lys Leu Asp Lys Cys
      20      25      30
Leu Ser Arg Tyr Gly Thr Arg Phe Glu Phe Asn Asn Glu Lys Gln Val
      35      40      45
Ile Phe Ser Ser Asp Val Asn Asn Glu Asp Thr Phe Val Ile Leu Glu
      50      55      60
Gly Val Ile Ser Leu Arg Arg Glu Glu Asn Val Leu Ile Gly Ile Thr
      65      70      75      80
Gln Ala Pro Tyr Ile Met Gly Leu Ala Asp Gly Leu Met Lys Asn Asp
      85      90      95
Ile Pro Tyr Lys Leu Ile Ser Glu Gly Asn Cys Thr Gly Tyr His Leu
      100      105      110
Pro Ala Lys Gln Thr Ile Thr Leu Ile Glu Gln Asn Gln Leu Trp Arg
      115      120      125

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Asp Ala Phe Tyr Trp Leu Ala Trp Gln Asn Arg Ile Leu Glu Leu Arg
 130          135          140
Asp Val Gln Leu Ile Gly His Asn Ser Tyr Glu Gln Ile Arg Ala Thr
 145          150          155          160
Leu Leu Ser Met Ile Asp Trp Asn Glu Glu Leu Arg Ser Arg Ile Gly
          165          170          175
Val Met Asn Tyr Ile His Gln Arg Thr Arg Ile Ser Arg Ser Val Val
          180          185          190
Ala Glu Val Leu Ala Ala Leu Arg Lys Gly Gly Tyr Ile Glu Met Asn
          195          200          205
Lys Gly Lys Leu Val Ala Ile Asn Arg Leu Pro Ser Glu Tyr
 210          215          220

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<210> 383
 <211> 84
 <212> PRT
 <213> E. Coli

```

<400> 383
Met Thr Asp Lys Ile Arg Thr Leu Gln Gly Arg Val Val Ser Asp Lys
 1          5          10          15
Met Glu Lys Ser Ile Val Val Ala Ile Glu Arg Phe Val Lys His Pro
          20          25          30
Ile Tyr Gly Lys Phe Ile Lys Arg Thr Thr Lys Leu His Val His Asp
          35          40          45
Glu Asn Asn Glu Cys Gly Ile Gly Asp Val Val Glu Ile Arg Glu Cys
          50          55          60
Arg Pro Leu Ser Lys Thr Lys Ser Trp Thr Leu Val Arg Val Val Glu
 65          70          75          80
Lys Ala Val Leu

```

<210> 384
 <211> 63
 <212> PRT
 <213> E. Coli

```

<400> 384
Met Lys Ala Lys Glu Leu Arg Glu Lys Ser Val Glu Glu Leu Asn Thr
 1          5          10          15
Glu Leu Leu Asn Leu Leu Arg Glu Gln Phe Asn Leu Arg Met Gln Ala
          20          25          30
Ala Ser Gly Gln Leu Gln Gln Ser His Leu Leu Lys Gln Val Arg Arg
          35          40          45
Asp Val Ala Arg Val Lys Thr Leu Leu Asn Glu Lys Ala Gly Ala
 50          55          60

```

<210> 385
 <211> 136
 <212> PRT
 <213> E. Coli

```

<400> 385
Met Leu Gln Pro Lys Arg Thr Lys Phe Arg Lys Met His Lys Gly Arg
 1          5          10          15
Asn Arg Gly Leu Ala Gln Gly Thr Asp Val Ser Phe Gly Ser Phe Gly
          20          25          30
Leu Lys Ala Val Gly Arg Gly Arg Leu Thr Ala Arg Gln Ile Glu Ala

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      35              40              45
Ala Arg Arg Ala Met Thr Arg Ala Val Lys Arg Gln Gly Lys Ile Trp
  50              55              60
Ile Arg Val Phe Pro Asp Lys Pro Ile Thr Glu Lys Pro Leu Ala Val
  65              70              75              80
Arg Met Gly Lys Gly Lys Gly Asn Val Glu Tyr Trp Val Ala Leu Ile
      85              90              95
Gln Pro Gly Lys Val Leu Tyr Glu Met Asp Gly Val Pro Glu Glu Leu
      100              105              110
Ala Arg Glu Ala Phe Lys Leu Ala Ala Lys Leu Pro Ile Lys Thr
      115              120              125
Thr Phe Val Thr Lys Thr Val Met
      130              135

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<210> 386
 <211> 233
 <212> PRT
 <213> E. Coli

```

      <400> 386
Met Gly Gln Lys Val His Pro Asn Gly Ile Arg Leu Gly Ile Val Lys
  1              5              10              15
Pro Trp Asn Ser Thr Trp Phe Ala Asn Thr Lys Glu Phe Ala Asp Asn
      20              25              30
Leu Asp Ser Asp Phe Lys Val Arg Gln Tyr Leu Thr Lys Glu Leu Ala
      35              40              45
Lys Ala Ser Val Ser Arg Ile Val Ile Glu Arg Pro Ala Lys Ser Ile
      50              55              60
Arg Val Thr Ile His Thr Ala Arg Pro Gly Ile Val Ile Gly Lys Lys
      65              70              75              80
Gly Glu Asp Val Glu Lys Leu Arg Lys Val Val Ala Asp Ile Ala Gly
      85              90              95
Val Pro Ala Gln Ile Asn Ile Ala Glu Val Arg Lys Pro Glu Leu Asp
      100              105              110
Ala Lys Leu Val Ala Asp Ser Ile Thr Ser Gln Leu Glu Arg Arg Val
      115              120              125
Met Phe Arg Arg Ala Met Lys Arg Ala Val Gln Asn Ala Met Arg Leu
      130              135              140
Gly Ala Lys Gly Ile Lys Val Glu Val Ser Gly Arg Leu Gly Gly Ala
      145              150              155              160
Glu Ile Ala Arg Thr Glu Trp Tyr Arg Glu Gly Arg Val Pro Leu His
      165              170              175
Thr Leu Arg Ala Asp Ile Asp Tyr Asn Thr Ser Glu Ala His Thr Thr
      180              185              190
Tyr Gly Val Ile Gly Val Lys Val Trp Ile Phe Lys Gly Glu Ile Leu
      195              200              205
Gly Gly Met Ala Ala Val Glu Gln Pro Glu Lys Pro Ala Ala Gln Pro
      210              215              220
Lys Lys Gln Gln Arg Lys Gly Arg Lys
      225              230

```

<210> 387
 <211> 110
 <212> PRT
 <213> E. Coli

<400> 387


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Met Glu Thr Ile Ala Lys His Arg His Ala Arg Ser Ser Ala Gln Lys
 1          5          10          15
Val Arg Leu Val Ala Asp Leu Ile Arg Gly Lys Lys Val Ser Gln Ala
          20          25          30
Leu Asp Ile Leu Thr Tyr Thr Asn Lys Lys Ala Ala Val Leu Val Lys
          35          40          45
Lys Val Leu Glu Ser Ala Ile Ala Asn Ala Glu His Asn Asp Gly Ala
          50          55          60
Asp Ile Asp Asp Leu Lys Val Thr Lys Ile Phe Val Asp Glu Gly Pro
65          70          75          80
Ser Met Lys Arg Ile Met Pro Arg Ala Lys Gly Arg Ala Asp Arg Ile
          85          90          95
Leu Lys Arg Thr Ser His Ile Thr Val Val Val Ser Asp Arg
          100          105          110

```

<210> 388
 <211> 92
 <212> PRT
 <213> E. Coli

```

<400> 388
Met Pro Arg Ser Leu Lys Lys Gly Pro Phe Ile Asp Leu His Leu Leu
 1          5          10          15
Met Lys Val Glu Lys Ala Val Glu Ser Gly Asp Lys Lys Pro Leu Arg
          20          25          30
Thr Trp Ser Arg Arg Ser Thr Ile Phe Pro Asn Met Ile Gly Leu Thr
          35          40          45
Ile Ala Val His Asn Gly Arg Gln His Val Pro Val Phe Val Thr Asp
          50          55          60
Glu Met Val Gly His Lys Leu Gly Glu Phe Ala Pro Thr Arg Thr Tyr
65          70          75          80
Arg Gly His Ala Ala Asp Lys Lys Ala Lys Lys Lys
          85          90

```

<210> 389
 <211> 273
 <212> PRT
 <213> E. Coli

```

<400> 389
Met Ala Val Val Lys Cys Lys Pro Thr Ser Pro Gly Arg Arg His Val
 1          5          10          15
Val Lys Val Val Asn Pro Glu Leu His Lys Gly Lys Pro Phe Ala Pro
          20          25          30
Leu Leu Glu Lys Asn Ser Lys Ser Gly Gly Arg Asn Asn Asn Gly Arg
          35          40          45
Ile Thr Thr Arg His Ile Gly Gly Gly His Lys Gln Ala Tyr Arg Ile
          50          55          60
Val Asp Phe Lys Arg Asn Lys Asp Gly Ile Pro Ala Val Val Glu Arg
65          70          75          80
Leu Glu Tyr Asp Pro Asn Arg Ser Ala Asn Ile Ala Leu Val Leu Tyr
          85          90          95
Lys Asp Gly Glu Arg Arg Tyr Ile Leu Ala Pro Lys Gly Leu Lys Ala
          100          105          110
Gly Asp Gln Ile Gln Ser Gly Val Asp Ala Ala Ile Lys Pro Gly Asn
          115          120          125
Thr Leu Pro Met Arg Asn Ile Pro Val Gly Ser Thr Val His Asn Val

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130 135 140
 Glu Met Lys Pro Gly Lys Gly Gly Gln Leu Ala Arg Ser Ala Gly Thr
 145 150 155 160
 Tyr Val Gln Ile Val Ala Arg Asp Gly Ala Tyr Val Thr Leu Arg Leu
 165 170 175
 Arg Ser Gly Glu Met Arg Lys Val Glu Ala Asp Cys Arg Ala Thr Leu
 180 185 190
 Gly Glu Val Gly Asn Ala Glu His Met Leu Arg Val Leu Gly Lys Ala
 195 200 205
 Gly Ala Ala Arg Trp Arg Gly Val Arg Pro Thr Val Arg Gly Thr Ala
 210 215 220
 Met Asn Pro Val Asp His Pro His Gly Gly Gly Glu Gly Arg Asn Phe
 225 230 235 240
 Gly Lys His Pro Val Thr Pro Trp Gly Val Gln Thr Lys Gly Lys Lys
 245 250 255
 Thr Arg Ser Asn Lys Arg Thr Asp Lys Phe Ile Val Arg Arg Arg Ser
 260 265 270
 Lys

<210> 390
 <211> 100
 <212> PRT
 <213> E. Coli

<400> 390
 Met Ile Arg Glu Glu Arg Leu Leu Lys Val Leu Arg Ala Pro His Val
 1 5 10 15
 Ser Glu Lys Ala Ser Thr Ala Met Glu Lys Ser Asn Thr Ile Val Leu
 20 25 30
 Lys Val Ala Lys Asp Ala Thr Lys Ala Glu Ile Lys Ala Ala Val Gln
 35 40 45
 Lys Leu Phe Glu Val Glu Val Glu Val Val Asn Thr Leu Val Val Lys
 50 55 60
 Gly Lys Val Lys Arg His Gly Gln Arg Ile Gly Arg Arg Ser Asp Trp
 65 70 75 80
 Lys Lys Ala Tyr Val Thr Leu Lys Glu Gly Gln Asn Leu Asp Phe Val
 85 90 95
 Gly Gly Ala Glu
 100

<210> 391
 <211> 201
 <212> PRT
 <213> E. Coli

<400> 391
 Met Glu Leu Val Leu Lys Asp Ala Gln Ser Ala Leu Thr Val Ser Glu
 1 5 10 15
 Thr Thr Phe Gly Arg Asp Phe Asn Glu Ala Leu Val His Gln Val Val
 20 25 30
 Val Ala Tyr Ala Ala Gly Ala Arg Gln Gly Thr Arg Ala Gln Lys Thr
 35 40 45
 Arg Ala Glu Val Thr Gly Ser Gly Lys Lys Pro Trp Arg Gln Lys Gly
 50 55 60
 Thr Gly Arg Ala Arg Ser Gly Ser Ile Lys Ser Pro Ile Trp Arg Ser
 65 70 75 80

Gly Gly Val Thr Phe Ala Ala Arg Pro Gln Asp His Ser Gln Lys Val
 85 90 95
 Asn Lys Lys Met Tyr Arg Gly Ala Leu Lys Ser Ile Leu Ser Glu Leu
 100 105 110
 Val Arg Gln Asp Arg Leu Ile Val Val Glu Lys Phe Ser Val Glu Ala
 115 120 125
 Pro Lys Thr Lys Leu Leu Ala Gln Lys Leu Lys Asp Met Ala Leu Glu
 130 135 140
 Asp Val Leu Ile Ile Thr Gly Glu Leu Asp Glu Asn Leu Phe Leu Ala
 145 150 155 160
 Ala Arg Asn Leu His Lys Val Asp Val Arg Asp Ala Thr Gly Ile Asp
 165 170 175
 Pro Val Ser Leu Ile Ala Phe Asp Lys Val Val Met Thr Ala Asp Ala
 180 185 190
 Val Lys Gln Val Glu Glu Met Leu Ala
 195 200

<210> 392
 <211> 209
 <212> PRT
 <213> E. Coli

<400> 392
 Met Ile Gly Leu Val Gly Lys Lys Val Gly Met Thr Arg Ile Phe Thr
 1 5 10 15
 Glu Asp Gly Val Ser Ile Pro Val Thr Val Ile Glu Val Glu Ala Asn
 20 25 30
 Arg Val Thr Gln Val Lys Asp Leu Ala Asn Asp Gly Tyr Arg Ala Ile
 35 40 45
 Gln Val Thr Thr Gly Ala Lys Lys Ala Asn Arg Val Thr Lys Pro Glu
 50 55 60
 Ala Gly His Phe Ala Lys Ala Gly Val Glu Ala Gly Arg Gly Leu Trp
 65 70 75 80
 Glu Phe Arg Leu Ala Glu Gly Glu Glu Phe Thr Val Gly Gln Ser Ile
 85 90 95
 Ser Val Glu Leu Phe Ala Asp Val Lys Lys Val Asp Val Thr Gly Thr
 100 105 110
 Ser Lys Gly Lys Gly Phe Ala Gly Thr Val Lys Arg Trp Asn Phe Arg
 115 120 125
 Thr Gln Asp Ala Thr His Gly Asn Ser Leu Ser His Arg Val Pro Gly
 130 135 140
 Ser Ile Gly Gln Asn Gln Thr Pro Gly Lys Val Phe Lys Gly Lys Lys
 145 150 155 160
 Met Ala Gly Gln Met Gly Asn Glu Arg Val Thr Val Gln Ser Leu Asp
 165 170 175
 Val Val Arg Val Asp Ala Glu Arg Asn Leu Leu Leu Val Lys Gly Ala
 180 185 190
 Val Pro Gly Ala Thr Gly Ser Asp Leu Ile Val Lys Pro Ala Val Lys
 195 200 205
 Ala

<210> 393
 <211> 103
 <212> PRT
 <213> E. Coli

<400> 393

Met Gln Asn Gln Arg Ile Arg Ile Arg Leu Lys Ala Phe Asp His Arg
 1 5 10 15
 Leu Ile Asp Gln Ala Thr Ala Glu Ile Val Glu Thr Ala Lys Arg Thr
 20 25 30
 Gly Ala Gln Val Arg Gly Pro Ile Pro Leu Pro Thr Arg Lys Glu Arg
 35 40 45
 Phe Thr Val Leu Ile Ser Pro His Val Asn Lys Asp Ala Arg Asp Gln
 50 55 60
 Tyr Glu Ile Arg Thr His Leu Arg Leu Val Asp Ile Val Glu Pro Thr
 65 70 75 80
 Glu Lys Thr Val Asp Ala Leu Met Arg Leu Asp Leu Ala Ala Gly Val
 85 90 95
 Asp Val Gln Ile Ser Leu Gly
 100

<210> 394

<211> 118

<212> PRT

<213> E. Coli

<400> 394

Met Ala Arg Val Lys Arg Gly Val Ile Ala Arg Ala Arg His Lys Lys
 1 5 10 15
 Ile Leu Lys Gln Ala Lys Gly Tyr Tyr Gly Ala Arg Ser Arg Val Tyr
 20 25 30
 Arg Val Ala Phe Gln Ala Val Ile Lys Ala Gly Gln Tyr Ala Tyr Arg
 35 40 45
 Asp Arg Arg Gln Arg Lys Arg Gln Phe Arg Gln Leu Trp Ile Ala Arg
 50 55 60
 Ile Asn Ala Ala Ala Arg Gln Asn Gly Ile Ser Tyr Ser Lys Phe Ile
 65 70 75 80
 Asn Gly Leu Lys Lys Ala Ser Val Glu Ile Asp Arg Lys Ile Leu Ala
 85 90 95
 Asp Ile Ala Val Phe Asp Lys Val Ala Phe Thr Ala Leu Val Glu Lys
 100 105 110
 Ala Lys Ala Ala Leu Ala
 115

<210> 395

<211> 65

<212> PRT

<213> E. Coli

<400> 395

Met Pro Lys Ile Lys Thr Val Arg Gly Ala Ala Lys Arg Phe Lys Lys
 1 5 10 15
 Thr Gly Lys Gly Gly Phe Lys His Lys His Ala Asn Leu Arg His Ile
 20 25 30
 Leu Thr Lys Lys Ala Thr Lys Arg Lys Arg His Leu Arg Pro Lys Ala
 35 40 45
 Met Val Ser Lys Gly Asp Leu Gly Leu Val Ile Ala Cys Leu Pro Tyr
 50 55 60
 Ala
 65

<210> 396
 <211> 180
 <212> PRT
 <213> E. Coli

<400> 396
 Met Lys Gly Gly Lys Arg Val Gln Thr Ala Arg Pro Asn Arg Ile Asn
 1 5 10 15
 Gly Glu Ile Arg Ala Gln Glu Val Arg Leu Thr Gly Leu Glu Gly Glu
 20 25 30
 Gln Leu Gly Ile Val Ser Leu Arg Glu Ala Leu Glu Lys Ala Glu Glu
 35 40 45
 Ala Gly Val Asp Leu Val Glu Ile Ser Pro Asn Ala Glu Pro Pro Val
 50 55 60
 Cys Arg Ile Met Asp Tyr Gly Lys Phe Leu Tyr Glu Lys Ser Lys Ser
 65 70 75 80
 Ser Lys Glu Gln Lys Lys Lys Gln Lys Val Ile Gln Val Lys Glu Ile
 85 90 95
 Lys Phe Arg Pro Gly Thr Asp Glu Gly Asp Tyr Gln Val Lys Leu Arg
 100 105 110
 Ser Leu Ile Arg Phe Leu Glu Glu Gly Asp Lys Ala Lys Ile Thr Leu
 115 120 125
 Arg Phe Arg Gly Arg Glu Met Ala His Gln Gln Ile Gly Met Glu Val
 130 135 140
 Leu Asn Arg Val Lys Asp Asp Leu Gln Glu Leu Ala Val Val Glu Ser
 145 150 155 160
 Phe Pro Thr Lys Ile Glu Gly Arg Gln Met Ile Met Val Leu Ala Pro
 165 170 175
 Lys Lys Lys Gln
 180

<210> 397
 <211> 642
 <212> PRT
 <213> E. Coli

<400> 397
 Met Pro Val Ile Thr Leu Pro Asp Gly Ser Gln Arg His Tyr Asp His
 1 5 10 15
 Ala Val Ser Pro Met Asp Val Ala Leu Asp Ile Gly Pro Gly Leu Ala
 20 25 30
 Lys Ala Cys Ile Ala Gly Arg Val Asn Gly Glu Leu Val Asp Ala Cys
 35 40 45
 Asp Leu Ile Glu Asn Asp Ala Gln Leu Ser Ile Ile Thr Ala Lys Asp
 50 55 60
 Glu Glu Gly Leu Glu Ile Ile Arg His Ser Cys Ala His Leu Leu Gly
 65 70 75 80
 His Ala Ile Lys Gln Leu Trp Pro His Thr Lys Met Ala Ile Gly Pro
 85 90 95
 Val Ile Asp Asn Gly Phe Tyr Tyr Asp Val Asp Leu Asp Arg Thr Leu
 100 105 110
 Thr Gln Glu Asp Val Glu Ala Leu Glu Lys Arg Met His Glu Leu Ala
 115 120 125
 Glu Lys Asn Tyr Asp Val Ile Lys Lys Lys Val Ser Trp His Glu Ala
 130 135 140
 Arg Glu Thr Phe Ala Asn Arg Gly Glu Ser Tyr Lys Val Ser Ile Leu
 145 150 155 160
 Asp Glu Asn Ile Ala His Asp Asp Lys Pro Gly Leu Tyr Phe His Glu
 165 170 175

Glu Tyr Val Asp Met Cys Arg Gly Pro His Val Pro Asn Met Arg Phe
 180 185 190
 Cys His His Phe Lys Leu Met Lys Thr Ala Gly Ala Tyr Trp Arg Gly
 195 200 205
 Asp Ser Asn Asn Lys Met Leu Gln Arg Ile Tyr Gly Thr Ala Trp Ala
 210 215 220
 Asp Lys Lys Ala Leu Asn Ala Tyr Leu Gln Arg Leu Glu Glu Ala Ala
 225 230 235 240
 Lys Arg Asp His Arg Lys Ile Gly Lys Gln Leu Asp Leu Tyr His Met
 245 250 255
 Gln Glu Glu Ala Pro Gly Met Val Phe Trp His Asn Asp Gly Trp Thr
 260 265 270
 Ile Phe Arg Glu Leu Glu Val Phe Val Arg Ser Lys Leu Lys Glu Tyr
 275 280 285
 Gln Tyr Gln Glu Val Lys Gly Pro Phe Met Met Asp Arg Val Leu Trp
 290 295 300
 Glu Lys Thr Gly His Trp Asp Asn Tyr Lys Asp Ala Met Phe Thr Thr
 305 310 315 320
 Ser Ser Glu Asn Arg Glu Tyr Cys Ile Lys Pro Met Asn Cys Pro Gly
 325 330 335
 His Val Gln Ile Phe Asn Gln Gly Leu Lys Ser Tyr Arg Asp Leu Pro
 340 345 350
 Leu Arg Met Ala Glu Phe Gly Ser Cys His Arg Asn Glu Pro Ser Gly
 355 360 365
 Ser Leu His Gly Leu Met Arg Val Arg Gly Phe Thr Gln Asp Asp Ala
 370 375 380
 His Ile Phe Cys Thr Glu Glu Gln Ile Arg Asp Glu Val Asn Gly Cys
 385 390 395 400
 Ile Arg Leu Val Tyr Asp Met Tyr Ser Thr Phe Gly Phe Glu Lys Ile
 405 410 415
 Val Val Lys Leu Ser Thr Arg Pro Glu Lys Arg Ile Gly Ser Asp Glu
 420 425 430
 Met Trp Asp Arg Ala Glu Ala Asp Leu Ala Val Ala Leu Glu Glu Asn
 435 440 445
 Asn Ile Pro Phe Glu Tyr Gln Leu Gly Glu Gly Ala Phe Tyr Gly Pro
 450 455 460
 Lys Ile Glu Phe Thr Leu Tyr Asp Cys Leu Asp Arg Ala Trp Gln Cys
 465 470 475 480
 Gly Thr Val Gln Leu Asp Phe Ser Leu Pro Ser Arg Leu Ser Ala Ser
 485 490 495
 Tyr Val Gly Glu Asp Asn Glu Arg Lys Val Pro Val Met Ile His Arg
 500 505 510
 Ala Ile Leu Gly Ser Met Glu Arg Phe Ile Gly Ile Leu Thr Glu Glu
 515 520 525
 Phe Ala Gly Phe Phe Pro Thr Trp Leu Ala Pro Val Gln Val Val Ile
 530 535 540
 Met Asn Ile Thr Asp Ser Gln Ser Glu Tyr Val Asn Glu Leu Thr Gln
 545 550 555 560
 Lys Leu Ser Asn Ala Gly Ile Arg Val Lys Ala Asp Leu Arg Asn Glu
 565 570 575
 Lys Ile Gly Phe Lys Ile Arg Glu His Thr Leu Arg Arg Val Pro Tyr
 580 585 590
 Met Leu Val Cys Gly Asp Lys Glu Val Glu Ser Gly Lys Val Ala Val
 595 600 605
 Arg Thr Arg Arg Gly Lys Asp Leu Gly Ser Met Asp Val Asn Glu Val
 610 615 620
 Ile Glu Lys Leu Gln Gln Glu Ile Arg Ser Arg Ser Leu Lys Gln Leu
 625 630 635 640
 Glu Glu

<210> 398
 <211> 450
 <212> PRT
 <213> E. Coli

<400> 398
 Met Thr Lys His Tyr Asp Tyr Ile Ala Ile Gly Gly Gly Ser Gly Gly
 1 5 10 15
 Ile Ala Ser Ile Asn Arg Ala Ala Met Tyr Gly Gln Lys Cys Ala Leu
 20 25 30
 Ile Glu Ala Lys Glu Leu Gly Gly Thr Cys Val Asn Val Gly Cys Val
 35 40 45
 Pro Lys Lys Val Met Trp His Ala Ala Gln Ile Arg Glu Ala Ile His
 50 55 60
 Met Tyr Gly Pro Asp Tyr Gly Phe Asp Thr Thr Ile Asn Lys Phe Asn
 65 70 75 80
 Trp Glu Thr Leu Ile Ala Ser Arg Thr Ala Tyr Ile Asp Arg Ile His
 85 90 95
 Thr Ser Tyr Glu Asn Val Leu Gly Lys Asn Asn Val Asp Val Ile Lys
 100 105 110
 Gly Phe Ala Arg Phe Val Asp Ala Lys Thr Leu Glu Val Asn Gly Glu
 115 120 125
 Thr Ile Thr Ala Asp His Ile Leu Ile Ala Thr Gly Gly Arg Pro Ser
 130 135 140
 His Pro Asp Ile Pro Gly Val Glu Tyr Gly Ile Asp Ser Asp Gly Phe
 145 150 155 160
 Phe Ala Leu Pro Ala Leu Pro Glu Arg Val Ala Val Val Gly Ala Gly
 165 170 175
 Tyr Ile Ala Val Glu Leu Ala Gly Val Ile Asn Gly Leu Gly Ala Lys
 180 185 190
 Thr His Leu Phe Val Arg Lys His Ala Pro Leu Arg Ser Phe Asp Pro
 195 200 205
 Met Ile Ser Glu Thr Leu Val Glu Val Met Asn Ala Glu Gly Pro Gln
 210 215 220
 Leu His Thr Asn Ala Ile Pro Lys Ala Val Val Lys Asn Thr Asp Gly
 225 230 235 240
 Ser Leu Thr Leu Glu Leu Glu Asp Gly Arg Ser Glu Thr Val Asp Cys
 245 250 255
 Leu Ile Trp Ala Ile Gly Arg Glu Pro Ala Asn Asp Asn Ile Asn Leu
 260 265 270
 Glu Ala Ala Gly Val Lys Thr Asn Glu Lys Gly Tyr Ile Val Val Asp
 275 280 285
 Lys Tyr Gln Asn Thr Asn Ile Glu Gly Ile Tyr Ala Val Gly Asp Asn
 290 295 300
 Thr Gly Ala Val Glu Leu Thr Pro Val Ala Val Ala Ala Gly Arg Arg
 305 310 315 320
 Leu Ser Glu Arg Leu Phe Asn Asn Lys Pro Asp Glu His Leu Asp Tyr
 325 330 335
 Ser Asn Ile Pro Thr Val Val Phe Ser His Pro Pro Ile Gly Thr Val
 340 345 350
 Gly Leu Thr Glu Pro Gln Ala Arg Glu Gln Tyr Gly Asp Asp Gln Val
 355 360 365
 Lys Val Tyr Lys Ser Ser Phe Thr Ala Met Tyr Thr Ala Val Thr Thr
 370 375 380
 His Arg Gln Pro Cys Arg Met Lys Leu Val Cys Val Gly Ser Glu Glu
 385 390 395 400
 Lys Ile Val Gly Ile His Gly Ile Gly Phe Gly Met Asp Glu Met Leu
 405 410 415
 Gln Gly Phe Ala Val Ala Leu Lys Met Gly Ala Thr Lys Lys Asp Phe
 420 425 430

Asp Asn Thr Val Ala Ile His Pro Thr Ala Ala Glu Glu Phe Val Thr
 435 440 445
 Met Arg
 450

<210> 399
 <211> 2894
 <212> RNA
 <213> E. Coli

<400> 399
 aagguaaagc cucacggguuc auuaguaccg guuagcucaa cgcaucgcug cguuacaca 60
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 aacucaucuc ggggcaaguu ucgugcuuag augcuuucag cacuuauuc uuccgcauuu 180
 agcuaccggg cagugccauu ggcaugacaa cccgaacacc agugaugcgu ccacuccggu 240
 ccucucguac uaggagcagc ccccccucagu ucuccagcgc ccacggcaga uagggaccga 300
 acugucucac gacguucuaa acccagcucg cguaccacuu uaaauggcga acagccauac 360
 ccuugggacc uacuucagcc ccaggauug augagccgac aucgaggugc caaacaccgc 420
 cgucgauaug aacucuuggg cgguaucagc cuguuauccc cggaguaccu uuuaucgguu 480
 gagcgauagg ccuuccauuc agaaccaccg gaucacuaug accugcuuuc gcaccugcuc 540
 gcgcgcgucac gcucgcaguc aagcuggcuu augccaauug acuaaccucc ugauguccga 600
 ccaggauuag ccaaccuucg ugcuccuccg uuacucuuaa ggaggagacc gcccaguca 660
 aacuaaccac cagacacugu ccgcaaccgg gauuacgggu caacguuaga acauaaaca 720
 uuaaagggug guuuuuaag gucggcuca ugcagacug cguccacacu ucaaagccuc 780
 ccaccuaucc uacacaucaa ggcucaaugu ucagugucaa gcuaauagua agguucacgg 840
 ggucuauccg ucugcccgcg gguacacugc aucuucacag cgaguucau uucacugagu 900
 cucgggugga gacagccugg ccacauuac gccauucgug caggucggaa cuuaccgcac 960
 aaggaauuuc gcuaccuuag gaccguuaa guuacggccg ccguuuaccg gggcuucgau 1020
 caagagcuuc gcugccgcu aaccuacaa uuacccuucc ggaccgggc aggcgucaca 1080
 ccguauacgu ccacuuucgu guuugcacag ugcuguguuu uuaauaaca guugcagcca 1140
 gcugguauuc ucgacugau ucagcuccau ccgcgaggga ccuaccuac auaucagcgu 1200
 gccuucuccc gaaguacgg caccuuuug ccuaguuccu ucacccgagu ucucucaagc 1260
 gccuugguau ucucuaccug accaccugug ucgguuugg guacgauuug auguuaccug 1320
 augcuuagag gcuuuuccug gaagcagggc auuuuguugc ucagcaccgu agugccucgu 1380
 caucacgccc cagccuugau uuuccggau ugcucggaaa accagccuac acgcuuaaac 1440
 cgggacaacc gcugccgcu caacauagcc uucuccguc ccccuucgca guaacaccaa 1500
 guacaggaau auuaaccugu uucccaucga cuacgcguu ccccuucgca uuaggggucg 1560
 acucaccucg ccccgauuaa cguuggacag gaacccuug ucuccggcg agcgggcuuu 1620
 ucacccgcuu uaucguuacu uaugucagca uucgcacuuc ugauaccucc agcaugccuc 1680
 acagcacacc uucgcaggcu uacagaacgc uccccuacc acaacgcgu aagcgucgcu 1740
 gccgcagcuu cggugcaugg uuuaagcccc uuacauuc cgcgcaggcc gacucgacca 1800
 gugagcuauu acgcuuucuu uaaaugaugg cugcuucuaa gccacauc uggcugucug 1860
 ggcuuucca caucguuucc cacuuaacca ugacuuugg accuuagcug gcggucuggg 1920
 uuguuuuccu cuucacgacg gacguuagca cccgcgugu gucucccgug auaacauuc 1980
 ccgguaucg caguugcau cggguuggua agucgggag acccccuugc cgaaacagug 2040
 cucuacccc ggagaugaau ucacgaggcg cuaccuaau agcuuucggg gagaaccagc 2100
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 auuagucggu ucgguccucc aguuauguu acccaaccu caaccugccc auggcuaugau 2220
 caccggguu cgggcuuaa cccugcaacu uaacgcccag uuaagacucg guuucccuuc 2280
 ggcucccuu uucgguuaac cuugcuacag aauuaaguc gcugaccu uauacaaaag 2340
 guacgcaguc acacgccuaa gcgugcucc acugcuuga cguacacggu uucagguuc 2400
 uuucacucc ccucgcggg guucuuuucg ccuuuccuc acgguacug uucacuaucg 2460
 gucagucagg aguauuagc cuuggaggau ggucccccca uauucagaca ggauaccag 2520
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 gcucccgguu cgcucggcg uacuggggga aucucggug auuucuuuuc cucggggguc 2700
 uuagauguu caguuccccc gguucggcu auuaaccuau ggauucagu aaugauagug 2760
 ugucgaaca cacuggguu ccccauucgg aaucgcgg uuuaacggu ucauauacc 2820
 uuaccgacgc uauucgcaga uuagcacguc cuuauccg ucugacugcc agggcaucca 2880

ccguguacgc uuagucgcuu aacc

2894

<210> 400
 <211> 120
 <212> RNA
 <213> E. Coli

<400> 400
 augccugggca guucccuacu cucgcauggg gagacccac acuaccaucg gcgcuacggc 60
 guuucacuuc ugaguucggc auggggucag guggggaccac cgcgcuacgg ccgccaggca 120

<210> 401
 <211> 76
 <212> RNA
 <213> E. Coli

<400> 401
 gucccuucg ucuagaggcc caggacaccg cccuucacg gcgguaacag gguuucgaau 60
 cccuagggg acgcca 76

<210> 402
 <211> 1549
 <212> RNA
 <213> E. Coli

<400> 402
 aaaauagaaga guuugaucu ggcucagauu gaacgcuggc ggcaggccua acacaugcaa 60
 gucgaacggg aacaggaagc agcuugcugc uucgcugacg aguggcggac gggugaguua 120
 ugucugggaa gcugccugau ggagggggau aacuacugga aacgguagcu aaauaccgcau 180
 aaugucgcaa gaccaaagag ggggaccuuc gggccucuu ccaucggaug ugcccagaug 240
 ggaauagcuu guugguuggg uaacggcuca ccaaggcgac gaucccuagc uggucugaga 300
 ggaugaccag ccacacugga acugagacac gguccagacu ccuacgggag gcagcagugg 360
 ggaauauugc acaauuggcg caagccugau gcagccaugc cgcguguaug aagaaggccu 420
 ucggguugua aguuacuuuc agcggggagg aaggagaua aguuauuacc uuugcuauu 480
 gacguuaccc gcagaagaag caccggcuua cuccgugcca gcagccgcgg uauuacggag 540
 ggugcaagcg uuauucggaa uuacugggcg uaaagcgac gcagggcggu ugguaaguc 600
 agaugugaaa ucccggggcu caaccugggg acugcaucug auacuggcaa gcuugagucu 660
 cguagagggg gguagaauuc cagguguagc ggugaaaugc guagagaucu ggaggauuac 720
 cggugggcgaa ggcggcccc uggacgaaga gcagcgcuca ggugcgaaag cguggggagc 780
 aaacaggauu agauaccug guaguccacg ccguaaacga ugucgacuug gagguugugc 840
 ccuugagggc ugguuuccgg agcuacggc uuaagucgac cggcggggg guacggccgc 900
 aagguuuuuu cucaauugaa uugacggggg cccgcacaag cgguggagca ugugguuuua 960
 uucgaugcaa cgcgaagaac cuuaccuggu cuugacauc accggaaguu ucagagauga 1020
 gaaugugccu ucgggaaccg ugagacaggu gcugcauggc ugucguagc ucguuugug 1080
 aaauguuggg uuaagucccg caacgagcgc aaccuuuau cuuuguugc agcgguccgg 1140
 ccgggaacuc aaaggagacu gccagugaua aacuggagga agguuggggu gacgucaagu 1200
 cauauaggcc cuuacgacca ggguacaca cgugcuacaa uggcgcauac aaagagaagc 1260
 gaccucgcga gagcaagcgg accucauaa gugcguagua guccggauug gagucugcaa 1320
 cucgacucca ugaagucgga aucgcuagua aucguggauc agaaugccac ggugaauacg 1380
 ucccggggc uuquacacac cggccgucac accaugggag uggguugcaa aagaaguagg 1440
 uagcuuaacc uucgggaggg cgcuuaccac uuugugauuc augacugggg ugaagucgua 1500
 acaagguaac cguaggggaa ccugcgguug gaucaccucc uuaccuuua 1549

<210> 403
 <211> 17
 <212> DNA
 <213> Artificial
 <220>
 <223> Primer Oligonucleotide

<400> 403
 tgtttatcag accgctt 17

<210> 404
 <211> 18
 <212> DNA
 <213> Artificial
 <220>
 <223> Primer Oligonucleotide

<400> 404
 acaatttcac acagcctc 18

<210> 405
 <211> 159
 <212> DNA
 <213> Escherichia coli

<400> 405
 caggtggtat ggaaacccaa aatggagacg ggaagctgaa ccagatagtt actggaggtg 60
 atcaccagca gatgaaataa cgataaccag aacaacgcct tatagcggtg agtttgcgag 120
 aaaacgttca tattgtacct ttttgattaa ccattgggg 159

<210> 406
 <211> 640
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(640)
 <223> n = A,T,C or G

<400> 406
 ggggnccaaa gtgtttgggn cgggcaactg gaggcccaacc ttaanttngg ggaaattttt 60
 aanaaaaggc ggggatttgt nagccacggg ngattanttt anaataaatt aagtgttgcc 120
 ataaggggac aaagngaagg aagtggntat taanggannc gccaatgcga nttagggcag 180
 accattcggc cattcgctt cttggttatc gaagttcatc cagatagccg ttgccngacc 240
 gaccagattc gcttcnggca caaagcccca gtaacggctg tccgcgctgt tgcgcgggtt 300
 gtcgcccac atgaagtatt gtcccggagg aacaatccag gttgccagtt gttgccctgg 360
 ctgctggtaa tacatcccca cctgacccg cgcaatcggc actgtcagaa tgcggtgcgt 420
 cacatcaccc agtgtctctt tacgctcgga aagacgaatt ccattttctt tggtttcgtt 480
 tttcggcact tcaaagaatc cgctggtcgc ttccccacca ttacggcgtg agaaggtctg 540
 aacgaaatcg ctcggttcca cgtttgagta ggtgaccggc agcgcgtttt cacacgcctg 600
 gccggaactg catcccgggt gaatcgtcag ctcttttgag 640

<210> 407
 <211> 682
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature

<222> (1)...(682)

<223> n = A,T,C or G

<400> 407

cctgcagggg	aatgtcgcca	ttaaactggc	gcaggcagcc	aaagagttgc	tccgcttcta	60
cccagtcggc	agcgacaact	tgcgttaaag	tcgcaaaatt	atcatctgca	ctcactgcgt	120
gacgtaagcg	gatggagtgg	ccggaaacct	catagtacc	gcccaccagt	tggcctgcat	180
cgctttgtag	cgtacgcgcg	gcattggcaa	taagattcag	atactcagac	tcttccgggg	240
ccttcgccag	cataaaagag	gaggatgctc	gcgtatgcag	caactgctcc	agcgcaaatt	300
gcagcccgcg	ttgagtatca	ctgaataaag	gatcgttttc	gtcaatcaaa	tgtggctgag	360
caaatatttc	ctgatagcta	tcggtatcag	gaaccagggtc	acgccatgca	agtttcgtaa	420
tgggtcaaagt	tgatgttttt	tagtctgttg	tcaaagccgc	nattataccn	gtaaccggca	480
ctacagcaca	cgtagaaagc	acccgacaat	actcctggca	tgggcgttaa	agctcacagg	540
atggagatct	tttcttctact	ggcctaaaaa	gctgatattc	tgtaaagagt	tacacngtaa	600
cattgagatc	gctatgaaat	atcaacaact	tggaaaatct	tgnaaagcng	gttggaaaat	660
ggaaagtatc	tggttaagaa	gc				682

<210> 408

<211> 309

<212> DNA

<213> Escherichia coli

<400> 408

ggggatccgg	cagaatttta	cgctgaccaa	tgacgcgacg	acgtggcatg	gaaatactcc	60
gttggttaatt	caggattgtc	caaaactcta	cgagtttagt	ttgacattta	agttaaaacg	120
tttggcctta	cttaacggag	aaccattaag	ccttaggacg	cttcacgcca	tacttggaa	180
gagcctgctt	acgggtcttta	acgccggagc	agtcaagcgc	accacgtacg	gtgtggtaac	240
gaacacccgg	gaggtcttta	acacgaccgc	cacggatcag	gatcacggag	tgctcctgca	300
gccaaagctt						309

<210> 409

<211> 1167

<212> DNA

<213> Escherichia coli

<400> 409

gtcgacccat	ctgtccattg	agcggacagt	ttgtgcaaca	ctattttggt	gaccggaaaa	60
tggaacactt	tcgcgaatgc	ctgttgctat	cacgcttaaa	ccatttcatt	gcgatttaca	120
cagaacggac	gtcctgtcgc	agtatatata	gtcgtcgata	gaaacaagca	ttgaaaggca	180
cagcagtagt	caaacagtgt	gaaacgctac	tggcgcctta	cagcgcaaaa	aggctgggtga	240
ctaaaaagtc	accagccatc	agcctgattt	ctcaggctgc	aaccggaagg	gttggcttat	300
ttaacttcaa	cttcagcgcc	agcttcttcc	agagcttttt	tcagtgtctc	tgcgtcgtct	360
ttgctcacgc	cttctttcag	agcagccggt	gcagattcta	ccaggctctt	agcttctttc	420
agacccaggc	cagttgcgcc	acgtactgct	ttgataacag	caactttggt	agcgccagca	480
gctttcagaa	ttacgtcgaa	ttcagttttt	tcttcaggag	cttcaaccgg	gccagcagct	540
acagctacag	cagcagcagc	ggaaacaccg	aatttttctt	ycattgcaga	gatcaagttc	600
tacaacgtcc	attacagaca	tagctgcaac	tgcttcaatg	awttgatctt	tagtgataga	660
catttaaatk	gttcctgaat	atcagaataa	gtttatacgt	aagcgaatgc	gttaaaaaga	720
taactgcgaw	taagcagctt	ytctcgcatc	gcgtacagma	gccagagtac	gaaccagttt	780
gccagccgaa	gcttctttca	tggttgccat	caggcgtgca	attgcttctt	cgtaggtcgg	840
cagagttgcc	aggcggtcga	tctgagacgc	cgggatcagc	tcaccttcaa	aggcagcgcc	900
tttgacctca	aattttgcat	tcgctttcgc	gaactctttg	aacagacgag	cagcagcgcc	960
cgggtgttcc	atagagtatg	caatcagggt	cggaccaaca	aacgcgtctt	tcaggcactc	1020
gaacggagta	ccttcaacag	cacggcgagc	cagggtgtta	cgaacaacac	gcatgtatac	1080
gccagcttcg	cgacctgctt	tacgcagttc	agtcatttta	tctacagtta	cgcccacggg	1140
aatccgcaac	tactgcaagc	caagctt				1167

<210> 410

<211> 404

<212> DNA

<213> Escherichia coli

<400> 410
 caacmctatt ttgktggacc ggaaaaakgga acacttttccg cawkgcctgt tgctatcacg 60
 cttaaaccat ttcattgcga ttacacaga acggacgtcc tgtcgcagta tattaagtcg 120
 tcgatagaaa caagcattga aaggcacagc agtagtcaaa cagtgtgaaa cgctactggc 180
 gccttacagc gcaaaaaggc tgggtgactaa aaagtcacca gccatcagcc tgattttctca 240
 ggctgcaacc ggaagggttg gcttatttaa cttcaacttc agcgccagct tcttccagag 300
 cttttttcag tgcttctgcg tcgtctttgc tcacgccttc tttcagagca gccggtgcag 360
 attctaccag gtcttttagct tctttcagac ccaggccagt tgcg 404

<210> 411
 <211> 152
 <212> DNA
 <213> Escherichia coli

<400> 411
 agagcttttt tcaagtcttc tgcgtcgtct ttgctcacgc cttctttcaa gagcagcccg 60
 gtgcagattc taccaggctt ttagcttctt tcagaccag gccagttgcg ccacgtactg 120
 ctttgataac agcaactttg ttagcgccag ca 152

<210> 412
 <211> 825
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(825)
 <223> n = A,T,C or G

<400> 412
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 gaaaatggaa cactttccgc aatgcctgtt gctatcacgc ttaamccatt tcattgcgat 120
 ttacacagaa cggacgtcct gtcgcagtat attaatgcgt cgatagaaac aagcattgaa 180
 aggcacagca gtagtcaaac agtgtgaaac gctactggcg ccttacagcg caaaaaggct 240
 ggtgactaaa aagtcaccag ccatcagcct gattttctcag gctgcaaccg gaagggttgg 300
 cttattttaac tcaacttca ggcagcgtt cttccagagc ttttttcagt gcttctgcgt 360
 cgtctttgct cagccttctt ttcagagcag ccgggtgcag attctaccag gtcttttagct 420
 tctttcagac ccaggccagt tgcgccacgt actgctttga taacagcaac tttgttagcg 480
 ccagcagctt tcagaattac gtcgaattca agttttttct tcagcagctt caaccgggcc 540
 agcagctaca gctacagcag cagcagcgga aacaccgaat ttttcttyca ttggcagaga 600
 tcaagttcta caacgtccat tacagacata gctgcaactg cttcaatgat tkgatcttwa 660
 gtgatagaca tttaaattgt tcctgaatat cagaataagt ttatacgtaa gcgaatgcgt 720
 taaaaagata actgcgatta agcagcttct ttcgcategc gtacagcagc cagaggtcga 780
 accagtttgc cagccgaagg ttggcttttc agcctnnnch natta 825

<210> 413
 <211> 425
 <212> DNA
 <213> Escherichia coli

<400> 413
 agtagtcaaa caggtgkgra acgctactgg cgccttacag cgcaaaaagg ctggtgacta 60
 aaaagtcacc agccatcarg ctgattttctc aggtctgcaac ccggaagggt tggtttattt 120
 aacttcaact tcagcgccag cttcttccag agcttttttc agtgcttctg cgctcgtctt 180
 gctcacgcct tctttcagag cagccgggtgc agattctacc aggtcttttag cttctttcag 240
 acccaggcca gttgcgccac gtactgcttt gataacagca actttgttag cgccagcagc 300
 tttcagaatt acgtcgaatt cagttttttc ttcagcagct tcaaccgggc cagcagctac 360
 agctacagca gcagcagcgg aaacacccga atttttcttc cattgcagag atcaagttct 420
 acaac 425

<210> 414
 <211> 126
 <212> DNA
 <213> Escherichia coli

<400> 414
 agagcttttt tcaagtgttc tgcgtcgtct ttgctcacgc cttctttcag agcagccggt 60
 gcagattcta ccagggtcttt agcttctttc agaccagcagc cagttgcgcc acgtactgct 120
 ttrata 126

<210> 415
 <211> 264
 <212> DNA
 <213> Escherichia coli

<400> 415
 ctgcmaccgg gargggttgg cttattttaac ttcaacttca gcgccagctt cttcagagc 60
 ttttttcaag tgcttctgcg tcgtctttgc tcacgccttc tttcagagca gccggtgcag 120
 attctaccag gtcttttagct tctttcagac ccaggccagc tgcgccacgt actgctttga 180
 taacagcaac tttgttagcg ccagcagctt tcagaattac gtcgaattca gttttttctt 240
 cagcagcttc aaccggggcca gcag 264

<210> 416
 <211> 201
 <212> DNA
 <213> Escherichia coli

<400> 416
 cgcataccct gcagcatcgg cccgatggag atcaggctcg cagaacgctg taccgctttg 60
 taggtggtgt taccgggtgt cagatccggg aagatgaaca cggtagcgcg acctgcaacc 120
 ggagagttcg gcgctttgga tttcgcaacg tcagccatta ccgcagcgtc gtactgcagc 180
 ggaccgtcga tcatcaggtc a 201

<210> 417
 <211> 239
 <212> DNA
 <213> Escherichia coli

<400> 417
 aattcagcag ttgacagtgg cataaacgta actggtgact tttgcccggc atgacgccgg 60
 gcttttttta ttattccgtg acttcacgag tagtgaaggc aaacttctcg ccatcaaata 120
 gccctgact ggtagtttt agcgcgggga tcaactggcag agaaagaaac gccatctgaa 180
 taaacggctc atcgggtaac ggaccgcatt cacgggcggc ggctttcaag gcgtcaatt 239

<210> 418
 <211> 223
 <212> DNA
 <213> Escherichia coli

<400> 418
 ttcttttttt cgtcaacggt gtccagaatc attttattta cctcgggtac ttatgctgat 60
 ttttattatt atggggaagg tgttatttat gagtttcatt tatgccgtaa cgacaatgaa 120
 ctgcgggaatt agtataagca gcgcgagaat aataatcatt gtgcaaatgc taatttaatt 180
 aatactattt aaatattatt ttgagcatat gcacataagg ttg 223

<210> 419
 <211> 223
 <212> DNA
 <213> Escherichia coli

<400> 419

ttcttttttt	cgtcaacggt	gtccagaatc	attttattta	cctcgggtac	ttatgctgat	60
ttttattatt	atggggaagg	tggtatttat	gagtttcatt	tatgccgtaa	cgacaatgaa	120
ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	gtgcaaatgc	taatttaatt	180
aatactattt	aatattatt	ttgagcatat	gcacataagg	ttg		223

<210> 420

<211> 212

<212> DNA

<213> Escherichia coli

<400> 420

aatagcgggt	atgcacgcct	ttcttttttt	cgtcaacggt	gtccagaatc	attttattta	60
cctcgggtac	ttatgctgat	ttttattatt	atggggaagg	tggtatttat	gagtttcatt	120
tatgccgtaa	cgmcaatgaa	ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	180
gtgcaaatgc	taatttaatt	aatactattt	aa			212

<210> 421

<211> 438

<212> DNA

<213> Escherichia coli

<400> 421

ccctgtaaat	tatcgcccg	ggcataaaaa	ctgcgtccaa	acgccgtctt	tgccagcagc	60
caggccataa	atgccaccag	aattatcgct	aaccaaccaa	ttgctgaaac	gccaagcagc	120
agcggggcgg	agagctgttt	cagttcggcg	ggtaaccctt	caatccattt	gccgccagtc	180
cacagcaaca	tgatgcctct	gtacaaccct	aacgtgccaa	gggtggcaac	aatggcaggg	240
atcttttagcc	acgcgaccag	gacaccgttg	aaaaatccc	cgagcaaacc	aagcagtaaa	300
gtcgcgacac	aagcaacagg	tagtgaatat	cctgcgttca	gtaacatccc	caacagcacc	360
gcgcacattc	cgggtaatcg	aaccccactt	gaaacatcaa	tattgsgsgt	aagcattwcc	420
aagcgttcgs	gcccattk					438

<210> 422

<211> 682

<212> DNA

<213> Escherichia coli

<400> 422

aattcccggg	gatccgctga	ccgtgcgctt	ccggttggtg	caaccgcgca	aatggcgcg	60
cggtaaagt	ggcgggggta	ttccttcccc	gttgaggaca	ccgggttgtc	agggtgacca	120
tacgcttaag	tgacaacccc	gctgcaacgc	cctctgttat	caattttctg	gtgacgtttg	180
gcggtatcag	ttttactccg	tgactgctct	gccgcccttt	ttaaagtga	ttttgtgatg	240
tggtgaatgc	ggctgagcgc	acgcggaaca	gttaaaacca	aaaacagtgt	tatgggtgga	300
ttctctgtat	ccggcggtta	ttgttaactg	gttaacgtca	cctggaggca	ccaggcactg	360
catcacaaaa	ttcattgttg	aggacgcgat	aatgaaaacg	ttattaccaa	acgttaatac	420
gtctgaaggt	tgttttgaaa	ttgggtgcac	tatcagtaac	ccagtattta	ctgaagatgc	480
cattaacaag	agaaaaaca	aacgggagct	attaaataaa	atatgcattg	tttcaatgct	540
ggctcgttta	cgtctgatgc	caaaaggatg	tgacacaatga	attcagcatt	tgtgcttggt	600
ctgacagttt	ttcttgtttc	cggagagcca	gttgatattg	cagtcagtgt	tcacaggaca	660
atgcaggagt	gatgactgca	gc				682

<210> 423

<211> 600

<212> DNA

<213> Escherichia coli

<400> 423

ggggatccga	ttgtgactgc	tctgccgccc	tttttaaagt	gaattttgtg	atgtggtgaa	60
tgccggtgag	cgcacgcgga	acagttaaaa	ccaaaaacag	tggtatgggt	ggattctctg	120
tatccggcgt	taattgttaa	ctgggttaacg	tcacctggag	gcaccaggca	ctgcatcaca	180
aaattcattg	ttgaggacgc	gataatgaaa	acgttattac	caaacgttaa	tacgtctgaa	240
ggttgctttg	aaattgggtg	cactatcagt	aaccagctat	ttactgaaga	tgccattaac	300

aagagaaaac	aagaacggga	gctattaaat	aaaatatgca	ttgtttcaat	gctggctcgt	360
ttacgtctga	tgccaaaagg	atgtgcacaa	tgaattcagc	atttgtgctt	gttctgacag	420
tttttcttgt	ttccggagag	ccagttgata	ttgcagtcag	tgttcacagg	acaatgcagg	480
agtgtatgac	tgacgaacc	gaacagaaaa	ttcccggtaa	ctgttaccog	gtcgataaag	540
ttattcacca	ggataatatc	gaaatcccgg	caggtcttta	aacagttccg	taataaataa	600

<210> 424

<211> 100

<212> DNA

<213> Escherichia coli

<400> 424

gggatccagc	aagaagatgc	ggttgtaccg	tcatacgcga	gatgcgcaaa	gctactcagc	60
aactgacctt	tcttcgcaat	aagcacgcca	ttagcgctcat			100

<210> 425

<211> 465

<212> DNA

<213> Escherichia coli

<400> 425

tcgcgtgttt	accttcaaca	tcggtaactt	tctggcggat	agtttcacgg	taagcaacct	60
gcggtttacc	tacgttcgct	tcaacgttga	attcacgctt	catacgggtca	acgatgatgt	120
cgagggtcag	ttcgcccata	cccgcgatga	tggtctggtt	agattcttcg	tcagtccata	180
cacggaaaaga	cgggtcttct	ttagccagac	ggcccagagc	cagaccattt	ttttcctggt	240
cagctttggt	tttcggttca	actgcgatgg	agattaccgg	ctcagggaat	tccatacggt	300
ccagaatgat	cggcgcatcc	gggtcacaca	gggtgtcacc	agtggttacg	tctttcagac	360
cgatagcagc	agcgatgtcg	cccgcgcgaa	cttctttgat	ctcttcacgt	ttgttagcgt	420
gcattctgaac	gatacgaccg	aaacgctcac	gtgcagcttt	cacgg		465

<210> 426

<211> 653

<212> DNA

<213> Escherichia coli

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 426

tgatcggctc	aagcagaact	ggtttcgctt	tcttaaagcc	ttctttaaag	gcgatagaag	60
cagccagttt	aaacgccagt	tcagaggagt	caacgtcatg	gtaagaaccg	aagtgcagac	120
gaatacccat	gtctactacc	gggtagcctg	ccagcggacc	tgctttcagc	tgttcctgga	180
tacctttatc	aacggccggg	atgtattcgc	cagggattac	accaccttta	atgtcgttga	240
tgaactcgta	gcctttcggg	tttgaaccgg	gctccagcgg	gtacatgtcg	ataacaacat	300
gaccatactg	accacgacca	ccagactggt	tcgcgtgttt	accttcaaca	tcggtaactt	360
tctggcggat	agtttcacgg	taagcaacct	gcggtttacc	tacgttcgct	tcaacgttga	420
attcacgctt	catacgggtca	acgatgatgt	cgagggtcag	ttcgccatac	ccgcgatgat	480
ggctgggtag	attcttcgct	agtccataca	cggnaagacg	ggtcttnttt	agccagacgg	540
gccagagnca	gacccatttt	tttctggcag	ctttggnntc	ggtcaactgc	gatggaaata	600
cccggctcaa	ggaattcata	cgtttcanaa	tgatcggggc	attccgggtc	aca	653

<210> 427

<211> 268

<212> DNA

<213> Escherichia coli

<400> 427

ctttcttaaa	gccttcttta	aaggcgatag	aagcagccag	tttaaacgcc	agttcagagg	60
agtcaacgtc	atggtaagaa	ccgaagtgca	gacgaatacc	catgtctact	accgggtagc	120

ctgccagcgg	acctgctttc	agctgttcct	ggataccttt	atcaacggcc	gggatgtatt	180
cgccagggat	tacaccacct	ttaatgtcgt	tgatgaactc	gtagcctttc	gggtttgaac	240
ccggctccag	cgggtacatg	tcgataac				268

<210> 428

<211> 330

<212> DNA

<213> Escherichia coli

<400> 428

gttttgggga	gatgtaagg	ctaattctgaa	tggtgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgatccttc	tgttcttata	acacaaggaa	acgtacttaa	ggcgctccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggtgtaag	gcttcccagt	300
aataataatta	atactctact	tccagagtag				330

<210> 429

<211> 465

<212> DNA

<213> Escherichia coli

<400> 429

gttttgggga	gatgtaagg	ctaattctgaa	tggtgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgatccttc	tgttcttata	acacaaggaa	acgtacttaa	ggcgctccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggtgtaag	gcttcccagt	300
aataataatta	atactctact	tccagagtag	aatattaaat	ttatccgcg	tggtgcatca	360
gcacaaattt	atcccacaac	tggtcttctg	tctcgacatg	cgcgggatct	ttcacaatag	420
tattggggat	cgggcacacc	ttctggcagg	ttggtgtctc	gtagt		465

<210> 430

<211> 379

<212> DNA

<213> Escherichia coli

<400> 430

aatctgaatg	gctgcattcc	ttgtttaagg	aaaaacgaat	gactgattgc	cgatacctga	60
ttaaaccggg	catcaaaatc	atcattgctg	ttttacagct	gatccttctg	ttcttataac	120
acaaggaaac	gtacttaagg	tgcgctccgt	gaaccagtcg	gacgcacctt	taataactat	180
aaataagtgt	ctgggcagat	actatataaa	ttaacttagt	gaatgattat	gctaattgtca	240
tcaattaaat	aaatataatg	gcgttaaggc	ttcccagtaa	tataattaat	actctacttc	300
cagagtagaa	tattaaattt	tatccgcgtg	gtgcacagc	acaaatttat	cccacaactg	360
ttcttctgtc	tcgacatgc					379

<210> 431

<211> 443

<212> DNA

<213> Escherichia coli

<400> 431

aagatgatgt	gatgagaaag	tcaatttgaa	taagacaata	ttaagagcta	aaaaaatgtc	60
aaaaaacact	aaatcaaaaa	ataatggcat	tagaaaaat	aatgcgaaaa	cggaggtgaa	120
attagtttat	ttcaaatgag	gaaaatctcc	cggcgaaaaa	accgggagat	gaaagtgtga	180
tggttatcaa	ataaacaaca	gaggagaaat	ttttaacgca	gccattcagg	caaactcgtt	240
aatcccattg	cctggcggat	aagttgcggc	ttaacgccag	gaagcgtgtc	ggccagtttc	300
aaaccaatat	cacgcagcag	ttttttcgcc	ggattgttac	cggaaaaacag	atcgcggaat	360
ccctgcatac	cagccagcat	caacgccgca	ctgtgcttgc	ggctacgctc	atagcgacgc	420
agataaatgt	actgcccgat	gtc				443

<210> 432
 <211> 638
 <212> DNA
 <213> Escherichia coli

<400> 432
 caggggggttt gttgtgggca atgatgcatt taagttatcg tctgcagata gaggagatat 60
 tacaataaac aacgaatcag ggcatttgat agtcaatacc gcaattctat caggagatat 120
 agtcactcta agaggaggag aaattagggt ggtattatag ctgtgctgag ccatgattgg 180
 cgcgcaattt aaacttagtg ctttacatcg ctattgtctt gatctctttg aattatttta 240
 taaattaaaa aaacgactgt tatgtataag caaagggtccg aacgaaaaat acattccaaa 300
 taaatgcttg cttaaatctc tatatccttc cccgaaaaat gacacataaa attgagatat 360
 tccaaaaaga gatactacaa ataaagatgc ctttatttta ttatttctaa taaaaataga 420
 agcaataaaa aataataaca atgatataaa tctaattgtt ttaaataat tgtcttttat 480
 gtttagtaata gtcgttagta tgtttgattc tccatatatt acgtgtagtt ttttatatac 540
 atggaataaa ttttctttat actgagacat cacaccatca tcaaatggaa gtttgaagat 600
 ggtgcttggt ttgctaacca ataaaaagag tgcattcg 638

<210> 433
 <211> 299
 <212> DNA
 <213> Escherichia coli

<400> 433
 ctttacctgg catgatccac ttcgccagaa taccggcaat aagcccaaaa ataatccatg 60
 acagaatgcc cattgtttcc tcacttatct gttttgcatt agcgggtag tcgctgataa 120
 aaagcatagc acaacatcgg gagggcaaga tttgtgacga gcatcacgga gggttttttg 180
 cgatggcgca gaaattgcgc catcaacgat cagtgataat taccaaccac aaacatcatg 240
 ttcgttttcc gtgtcataag aacgtacggt attcaccaga tcttttatca cttcagccg 299

<210> 434
 <211> 388
 <212> DNA
 <213> Escherichia coli

<400> 434
 gaaaaaggag gcaatatcgg gttaaaggcat tagcccgacg aatacgtcgg gctacaaata 60
 ttattgtgct gcaggtgttt tagcgggttg ttgatccaca ggttctaact ggaagaccac 120
 atcgacctga tcatcaaaact gaatagcggc ctgctcgtaa gtttcctggg cggacaccgg 180
 cgcggcatcg gctttcatca tccgcacatc tgggctgggc tgatagtggg aaacatggta 240
 gcgcacgcta tataccggcc ccagtttacg atgaaagccg ttcgccagtt cctgcgcctg 300
 atgaatcgcg ttatcaatcg ctgccttacg cgctttgtct ttataggcat ccggctgcgc 360
 cacgcccagc gacacagaac gaattccc 388

<210> 435
 <211> 351
 <212> DNA
 <213> Escherichia coli

<400> 435
 ctatccttga tgaaaccgag agcaaagata ggtgattacg tcatggtttt acagaaaatt 60
 acagaaaaag gaggcaatat cgggtaaaag cattagcccg acgaatacgt cgggctacaa 120
 atattattgt gctgcaggtg ttttagcggg ttgttgatcc acaggttcta actggaagac 180
 cacatcgacc tgatcatcaa actgaatagc ggcctgctcg taagtctctt gggcggacac 240
 cggcgcggca tcggctttca tcatccgcac cattgggctg ggctgatagt tggaaacatg 300
 gtagcgcacg ctatataaccg gccccagttt acgatgaaag ccgttcgcca g 351

<210> 436
 <211> 762
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(762)
 <223> n = A,T,C or G

<400> 436
 aattatgaaa cactgtcttg aatcgtctga atgacgggga catttgcgag cacgcatcca 60
 gtaataacac aggaaactat tttatctacg cgtagcgat agactgcttg catggcgaaa 120
 ggaggtaagc cgacgatttc agcgggacgc tgaacggga aagccctcc cgaggaaagg 180
 gccataaata aggaaagggt catgatgaag ctactcatca tcgtggtgct cttagtcata 240
 agcttccccg cttactaaga ctaccagggc gggggaaaacc ccgctctacc ctactcctg 300
 aaagtatgcc ttcacgataa gattgtcaat ccgcaggctt tgtagtctgc gatcctgcca 360
 gcaaataattc tttgcgagtc gttacgcaat aatcacagag gaaactattt tattcacgcg 420
 ttagegatag actgcattca gggcgaaaagg aggtaaaggc atgatttcag cgggacgctg 480
 aaacgggaaa gcctctcccg gagaagaggg cttttaataa ggaaaggggt atgatgaagc 540
 acgtcatcat actggtgata ctcttagtga ttagcttcca ggcttactaa gaacaccagg 600
 gggaggggga aacctcttcc taacctcac ttctgaaatt ggggtgctatg acgtggcgt 660
 tactgcttan cgctaccagt ttgtctgcc tggcggtgt aacgccagat cggtagccgt 720
 ttgatattt taatgaaagc cgacaaatca atcanctga cg 762

<210> 437
 <211> 292
 <212> DNA
 <213> Escherichia coli

<400> 437
 cacatttgcg agcacgcac cagtaataac acaggaaact attttatcta cgcgttagcg 60
 atagactgct tgcattggcg aaggaggtaa gccgacgatt tcagcgggac gctgaaacgg 120
 gaaagccctc cccgaggaa gggccataaa taaggaaagg gtcattgatga agctactcat 180
 catcgtgggt ctcttagtca taagcttccc cgcttactaa gactaccagg gcgggggaaa 240
 ccccgctcta ccctcactcc tgaaagtatg ccttcacgat aagattgtca at 292

<210> 438
 <211> 631
 <212> DNA
 <213> Escherichia coli

<400> 438
 atttacactt tttacgaaat catgggatca ctaacaaaat atcgcttgct agttatattg 60
 tatggcagga aagatatgag actgatatta cagatcccca aagtggagag tttatgacca 120
 ttaaaaaata gatgttgctg ggtgcgcttt tgctggttac cagtgcgccc tgggccgcac 180
 cagccaccgc gggttcgacc aatacctcgg gaatttctaa gtatgagtta agtagtttca 240
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 300
 agtacaacat taagcagtg cagttgcgta acctgccgc gcctgatgcc gggacgcact 360
 ggacctatat gggtggcgag tacgtgttga tcagcgacac cgacggtaaa atcattaaag 420
 cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gaggggaaa 480
 tgcagacacc ttgttatttt ttattattag ccacttgctc gtcttgcttg ttattagtcg 540
 tatttcacgt tgattaatgc ggtgcctcc agtgccagc atttaacttt gtttgtatcg 600
 tagacgtagt aactggctgt tatcggaatt g 631

<210> 439
 <211> 566
 <212> DNA
 <213> Escherichia coli

<400> 439
 tatggcagga aagatatgag actgatatta cagatcccca aagtggagag tttatgacca 60
 ttaaaaaata gatgttgctg ggtgcgcttt tgctggttac cagtgcgccc tgggccgcac 120
 cagccaccgc gggttcgacc aatacctcgg gaatttctaa gtatgagtta agtagtttca 180
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 240

agtacaacat taagcagtgg cagttgctga acctgcccgc gctgatgcc gggacgcaact	300
ggacctatat ggggtggcgcg tacgtgttga tcagcgacac cgacggtaaa atcattaaag	360
cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gagggggaaa	420
tgcagacacc ttgttatttt ttattattag ccacttgctc gtcttgcttg ttattagtcg	480
tatttcacgt tgattaatgc gggtgcctcc agtgcgccag atttaacttt gtttgtatcg	540
tagacgtagt aactggctgt atcgaa	566

<210> 440

<211> 339

<212> DNA

<213> Escherichia coli

<400> 440

cgtattcaca tccttttgat tgggtgataac atgcgaatcg gtattatttt tccggttgta	60
atcttcatta cagcggctcg attttttagca tgggttttta ttggcggcta tgetgccccg	120
ggagcataaa gatgaaaaaa acaacgatta ttatgatggg tgtggcgatt attgtcgtac	180
tcggcactga gctgggatgg tggtaacgtc acctctaaaa aatagcaaag gctgcctgtg	240
tgcagccttt gtgcaattta agcgttaact tttaatcttc ctgtagataa atagcacgac	300
aatcgcacca ataacggcaa ccacgaagct gccaaaaatt	339

<210> 441

<211> 376

<212> DNA

<213> Escherichia coli

<400> 441

catgaatatt taaaaaggaa aacgacatga aaccgaagca cagaatcaac attctccaat	60
cataaaatat ttccgtggag cattttatta ttgaatatag aggtttaact ccggtaaaaa	120
acaaagaagc attgaatgca gggaaaaata atatggccat aaaaaacatc gaaagaaact	180
cttttaattt aacatgtaaa cgcattggtta atcctcatat cacgggtgga gtgttaagaa	240
catacataaa tggagtcattg ttttcccttt tccatttatc aagttcctgt tgccgtttta	300
gtccatctct aattgcatat ttttaatttt ctgataaatg gcattgagca tcgatttcat	360
ttaaaacaac tgtaca	376

<210> 442

<211> 446

<212> DNA

<213> Escherichia coli

<400> 442

ttacgatagc tattagtaaa aatataagag ttagctgtat tggtatgtct gtggcgaaat	60
tgactacctt cgtttttttg attaagaatg attttattat cgtaagttaa attacatgaa	120
tatttaaaaa ggaaaacgac atgaaaccga agcacagaat caacattctc caatcataaa	180
atatttccgt ggagcatttt attattgaat atagagggtt aactccggtg aaaaacaaag	240
aagcattgaa tgcagggaaa aataatatgg ccataaaaaa catcgaaaga aactctttta	300
atttaacatg taaacgcatg gttaatcctc atatcacggg tggagtgtta agaacataca	360
taaatggagt catgttttcc cttttccatt tatcaagttc ctgttgccgt ttagtccat	420
ctctaattgc atattttaat ttttct	446

<210> 443

<211> 388

<212> DNA

<213> Escherichia coli

<220>

<221> misc_feature

<222> (1)...(388)

<223> n = A,T,C or G

<400> 443

tcaccccggt gccgattttc aggcattcctg atttaactta gcacccgcaa cttaactaca	60
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ggaaaacaaa gagataaatg tctaatacctg atgcaaatacg agccgatttt ttaatcttta	120
cggactttta cccgcctggg ttattaattg cactgtnatc cgggcgttcg cccgctttaa	180
tcacaataagg ctgtgtagcc tgggcctggt tctctttcac ccgcgccaga gcggcagcaa	240
tcgcactttt atctttggct gcagggtgaa cggctgcgct cttatgtcgt tcaaggcgag	300
ccgctttttc gcgctccaga cgagcctggc gcgcttcgaa acgcgctttg gcttctgcgg	360
cncgcttttc ttcctgacga atagccgc	388

<210> 444

<211> 209

<212> DNA

<213> Escherichia coli

<400> 444

aattttaata acgctatctg cggataaagc agaatagggtg gttaacccca gacataaacc	60
gaggaaaata atgttattgt atttcataat ctattgttcc ttagcgacag attgctgtct	120
gctggttcag taaggtagca ggagaaactt caggaagctt gtactcgaca atacagtttg	180
agtttttatc tttgccccat gaaacctgt	209

<210> 445

<211> 341

<212> DNA

<213> Escherichia coli

<400> 445

catcctcaat accgttaaat gcaacccgaa cccccgttgt ccctttgctg cattcaactta	60
acgtaatctg aaaagggacg gctggacttg tgctaccggt cggttgaaat tgtctggcac	120
tgtttttttg gagatctacg gtaaaattaa gcgaatccga tgagactgtg cagccataat	180
cgaggacgcg cccgctaatt ttaataacgc tatctgcgga taaagcagaa taggtggtta	240
accccagaca taaaccgagg aaaataatgt tattgtattt cataatctat tgttccttag	300
cgacagattg ctgtctgctg gttcagtaga gtaccaggag a	341

<210> 446

<211> 697

<212> DNA

<213> Escherichia coli

<400> 446

agatttactg ccaattttccg gcagatcgga aagggttaam ccatattgat ccataagggt	60
acgaatcmcg ggctataccg ccaggcatgg cttaggccat ggcattaaat tccgcaaatt	120
cgggcgctga ttcttccac gcggttattt tggcacacac cagatccagc aagggtttt	180
caggatcggt gagcagcaga tgatctacca gttccagcgc ctgggtgtat tgctcctcgt	240
tctgaatacc cgccagaaaa ggtgccacag cagttagctt ttctcctgct tgcaagatgt	300
cggcaatcgc aatcattttt tccccttagt acgatgaaca gcggtaaaga aatcgtattc	360
tttatgcgtc ataacttcac gtatgtagca cttttgcgat tcaaaaaaga ccattgctac	420
aacacgtaat tcattgcccc caacattgaa aacataatgc ttatccagat atttgaagtt	480
atccagagat gggaatactg cttttaatga ctcagggttt ttgaaatata ccttagcaat	540
cgtgktcccc agagccacca actccgtttt atgttgccggg tattttttccg cagcatcttt	600
caatgctttt tgagttatca ggtgcattct tcatcacgtc cgtkgmcaaa ttggcaatat	660
gataacatcc gttgccagat tggcacggat gaattat	697

<210> 447

<211> 215

<212> DNA

<213> Escherichia coli

<400> 447

aattaataac ttttcgtag gcagtttttg gtgtgagttg caagagggga gactactgaa	60
taactcaagt tttataatcg aggggaaaaat ggtgatggcg ttcatagcaa aacgccctca	120
accataaagg tcgagggcgc ttaagatgtt aaaaaccgc tatccgttaa aaaacaatgt	180
tcaactaagg tcagtgcacat tgcgctaaaa aagcg	215

<210> 448
 <211> 395
 <212> DNA
 <213> Escherichia coli

<400> 448
 gcattattca tgagaaatgt gtatcgtaaa tcaactgaaa ttaacgcaac catttggtat 60
 ttaagggttta attatctgtg tgtgatattt tattgaatgt tttaaatatt gtttttattg 120
 gcattgctat aatattgggt atcatttgct gaatggattc agtcttaatg agtgggtttt 180
 taagggacag gcatagagta atgatacgtg tgcataacca acatctttac tcattatgtc 240
 attgaatgtt gacgctatgt gtttatgagg gagaggattt ttcagttgat ctggattgtt 300
 aaattcatat aatgcgcctt tgctcatgaa tggatgccag tatgtagtgg gaaattataa 360
 atattgaaat agtccaacta cttctttatt accaa 395

<210> 449
 <211> 641
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(641)
 <223> n = A,T,C or G

<400> 449
 ataatcaggt aagaaaaggt gcgcggagat taccgtgtgt tgcgatatat tttttagttt 60
 cgcgtggcaa tacatcagtg gcaataaaac gacatatcca gaaaaatata cactaagtga 120
 atgatatctt ccgatttatc ttaatcgttt atggataacg gcaaagggtc tcgttttttc 180
 ctatacttat tcagcactca caaataaagg aacgccaatg aaaattatac tctgggctgt 240
 attgattatt ttcctgattg ggctactggt ggtgactggc gtatttaaga tgatatttta 300
 aaattaatta atgtcatcag gtccgaaaat aacgagaata tttcagtcct tcctcctgtt 360
 gcgctcctgt catgtgcatt gcttcatata atcactggcg caaggagcgc cgcaggcgna 420
 gnntgcncgn cgnccacact naccatgc cgaacttcag aantgaaaac nccntaacnc 480
 cgatngtcgg cgggngcctc cccatgcnan agtangggaa ntgccangcg ncnnattaaa 540
 cgaaaaggctn attncaaaga ctgggccttn cntttatctg atgtttgtcg gagaacgctc 600
 tcctgagnan gacaaatncc gccgggagcg gatttgaacn t 641

<210> 450
 <211> 314
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(314)
 <223> n = A,T,C or G

<400> 450
 gaactacgag taagaatagc tncgaattcc cgtttatgga taacggcaaa gggcttcggt 60
 ttttcctata cttattcagc actcacaat aaaggaacgc caatgaaaat tatactctgg 120
 gctgtattga ttattttcct gattgggcta ctgggtggtg ctggcggtatt taagatgata 180
 ttttaaaatt aattaatgtc atcagggtccg aaaataacga gaatatttca gtctctcatc 240
 ctgttgcgct cctgtcatgt gcattgcttc atataatcac tggcgcaagg agcgcgcagg 300
 gggntntnnt cttt 314

<210> 451
 <211> 236
 <212> DNA
 <213> Escherichia coli

<400> 451

atatacacta agtgaatgat atcttccgat ttatcttaat cgtttatgga taacggcaaa	60
gggcttcgtt ttttccata cttattcagc actcacaat aaaggaacgc caatgaaaat	120
tatactctgg gctgtattga ttattttcct gattgggcta ctgggtgtga ctggcgtatt	180
taagatgata ttttaaaatt aattaatgtc atcaggtccg aaaataacga gaatat	236

<210> 452

<211> 418

<212> DNA

<213> Escherichia coli

<400> 452

cggagattac cgtgtgttgc gatataat ttagtttcgc gtggcaatac atcagtggca	60
ataaaacgac atatccagaa aaatatacac taagtgaatg atatcttcgc atttatctta	120
atcgtttatg gataacggca aagggttcgc tttttccta tacttattca gactcacaa	180
ataaaggaac gccaatgaaa attatactct gggctgtatt gattattttc ctgattgggc	240
tactggtggt gactggcgta ttttaagatga ttttttaaaa ttaattaatg tcatcaggtc	300
cgaataaac gagaatattt cagtctctca tcctgttgcg ctctgtcat gtgcattgct	360
tcatataatc actggcgcaa ggagcgcgca gggggcggcc aatcgccgcc gccccctg	418

<210> 453

<211> 551

<212> DNA

<213> Escherichia coli

<400> 453

aacaatttgc ccatgcgctc ggtcatgcgc tgcacgccc ggccattttg sgcgtccccg	60
cgaccgccat tcgactgtta atgggcgaat cttcagtact ggtattaggt ggacaacgcg	120
cgtgcctaa acggctggaa gaagcgggtt ttgcgtttcg ctggtacgat ttagaagagg	180
cgtggcgga tgctgttcgc tgatgtggtt tacagcaaac atccgccagt taactcccg	240
tggtacagga ttagtggctt tgcgcgataa gatcgtctgg tgaaagtcgg gtcaccatca	300
taactaactc tctgtctaaa cctctatcca gcattcctg agcaatacgc agggcttctt	360
cgtgtttgcc ctgcattgcg ccttcttcac gtaatctgtc agcaatggtc atcaagtttc	420
tccttttctt gtgggtgcgcg ttccgctatc tcaccaataa atgcacgaaa acgctgggca	480
tcctctgttt gtaatacgtg attaaacagg gcttttagct gtctgtcatt agtgktccct	540
gtaactagca g	551

<210> 454

<211> 93

<212> DNA

<213> Escherichia coli

<400> 454

tggcatctcg gtgttgccga tcttcatgat atccagcccc ccggaaactt cttcccaaac	60
ggttttgctg ttatccattg agtcacggaa ctg	93

<210> 455

<211> 232

<212> DNA

<213> Escherichia coli

<400> 455

cgtgccgaga tgatcctgta accatcatca gttgtgaagt agtgattcac gacttcaagg	60
cgcttttcaa aagggtat tggctttgac atattagggg ctattccatt tcatcgtcca	120
acaaaatggg tgcagtacat actcgttga aatcaacaca ggaggctggg aatgccgcag	180
aatatagat tactttcttt aatagtatt tgtttcacgc tttattttt ca	232

<210> 456

<211> 713

<212> DNA

<213> Escherichia coli

<220>

<221> misc_feature

<222> (1)...(713)

<223> n = A,T,C or G

<400> 456

ttagnggatn naangcccac ancctcgang gatctaggag gtagaatagc ttcgaattcc	60
ccagcagagc gcggccttct tcgtcagatt tcgcagtagt ggtaatggta atatccaaac	120
cacgaacgcg gtcgacttta tcgtagtcga tttctgggaa gatgatctgc tcacggacac	180
ccatgctgta gttaccacga ccgtcgaaag acttagcgga caggccacgg aagtcacgga	240
tacgaggtac agcaatagtg atcaggcgct caaagaactc ccacatgcgt tcgccacgca	300
gagttacttt acagccgata ggatagccct gacggatttt gaagcctgca acagatttgc	360
gtgcttttgt gatcagcggg ttttgaccgg agattgctgc caggctctgct gctgcgttat	420
ccagcagttt tttgtcagcg atcgcttcac caacacccat gttcagggtg atcttctcga	480
cccaggggac ttgcatgaca gaattgtagt taaactcagt catgagtttt ttaactactt	540
cgtctttgta gtaatcatgc agtttcgcca tcgtactact ccatgtcggg gaacgctctc	600
ctgagtagga caaatccgcc ggagccggat ttaacgttgc gaacaaccgn cccggagggg	660
tggnggcagg accccgccat aactggcagc attaaattaa gcagaaggcc atc	713

<210> 457

<211> 292

<212> DNA

<213> Escherichia coli

<400> 457

tgaacagcag agatacggcc agtgcgccca atgttttttg tcctttaaac ataacagagt	60
cctttaagga tatagaatag gggatatagc acgccagaat atcgtatttg attattgcta	120
gttttttagt ttgcttaaaa atattgttag ttttattaaa tgcaaaacta aattattggg	180
atcatgaatt tggtgtatga tgaataaaat ataggggggt atagatagac gtcattttca	240
taggggtata aatgcgacta ccatgaagtt ttaattgaa agtattgggt tg	292

<210> 458

<211> 282

<212> DNA

<213> Escherichia coli

<400> 458

ttattaaatg caaaactaaa ttattgggat catgaatttg ttgtatgatg aataaaatat	60
aggggggtat agatagacgt cattttcata gggttataaa tgcgactacc atgaagtttt	120
taattgaaag tattgggttg ctgataattt gagctgttct attcttttta aatatctata	180
taggtctgtt aatggatttt atttttacaa ttttttgtgt ttaggcataa aaaaatcaac	240
ccgcatatg aacggcgggt taaaatattt acaacttagc aa	282

<210> 459

<211> 300

<212> DNA

<213> Escherichia coli

<400> 459

tctgcgttcc gctaaaagggt gcaaatgctc aggacgttgc agcgttttgc gtgaccgctc	60
ggggaaggca aaattgcctc tgggaaagca ttgcgcgggg tccggcgctc atcaacaatc	120
ggggggcagc aaggggctga aacgggaaag cccctccga agaaggggcc ttgtataagg	180
aaagggttat gatgaagctc gtcatacatc tgggtgtgtt gttactgtta agtttccga	240
cttactaaca actcatcaga ggggggagaa atcctccctt acccttggtc ctttactcta	300

<210> 460

<211> 293

<212> DNA

<213> Escherichia coli

<400> 460

cggggtccgg	cgctcatcaa	caatcggggg	gcagcaaggg	gctgaaacgg	gaaagcccct	60
cccgaagaag	gggccttgta	taaggaaagg	gttatgatga	agctcgtcac	catactgggt	120
gtgttggttac	tggttaagttt	cccgaacttac	taacaactca	tcagaggggg	gagaaatcct	180
cccttaccct	tggttccttta	ctctaggttg	aaaaaacaac	agcgtcaata	ggcctgccat	240
gtacgaagcg	agatctgtga	accgctttcc	ggttagcctt	ttttatcctg	ttg	293

<210> 461

<211> 359

<212> DNA

<213> Escherichia coli

<400> 461

caacacagga	ggctgggaat	gccgcagaaa	tatagattac	tttctttaat	agtgatttgt	60
ttcacgcttt	tatttttcac	ctggatgata	agagattcac	tggtggaatt	gcatattaaa	120
caggagagtt	atgagctggc	ggcgttttta	gcctgcaa	tgaaagagta	agagtcttcg	180
gcgggaaatt	attcccgcct	tacttacggc	gttgcgcat	ctcattgcac	ccaaatttat	240
tcttcacaaa	aataataata	gattttatta	cgcgatcgat	tattttattc	ctgaaaacaa	300
ataaaaaaat	ccccgccaaa	tggcagggat	cttagattct	gtgcttttaa	gcagagatt	359

<210> 462

<211> 673

<212> DNA

<213> Escherichia coli

<400> 462

gcaacccatg	tcctgacctg	ggttcggggg	acacaaaaac	gtgccgagat	gatcctgtaa	60
ccatcatcag	ttgtgaagta	gtgattcacg	acttcaaggc	gcttttcaaa	agggattttt	120
ggctttgaca	tattaggggc	tattccattt	catcgtccaa	caaaatgggt	gcagtacata	180
ctcgttgga	atcaacacag	gaggctggga	atgccgcaga	aatatagatt	actttcttta	240
atagtgattt	gtttcacgct	tttatttttc	acctggatga	taagagattc	actgtgtgaa	300
ttgcatatta	aacaggagag	ttatgagctg	gcggcggttt	tagcctgcaa	attgaaagag	360
taagagtctt	cggcgggaaa	ttattcccgc	cttacttacg	gcgttgcgca	ttctcattgc	420
acccaaattt	attcttcaca	aaaataataa	tagattttat	tacgcgatcg	attattttatt	480
tcctgaaaac	aaataaaaaa	atccccgcca	aatggcaggg	atcttagatt	ctgtgctttt	540
aagcagagaa	tacaggctgg	ttacgttacc	agctgccggg	cctttagcgc	cgctttcgat	600
ggtgaaggac	actttctgac	cttcgtccag	agatttgtaa	ccatcgttct	ggatagcaga	660
gaagtgtacg	aac					673

<210> 463

<211> 630

<212> DNA

<213> Escherichia coli

<400> 463

tggtggcatt	ggttgctgga	gagagaaaac	ccccgcacgt	tgcaggtatg	cacctgacaa	60
caccacgggg	gctaattcttg	actctagacc	actcaagaat	agccgcgaaa	cgttgtcatt	120
acaacacagg	cggctatatg	acgttcgcag	agctgggcat	ggccttcttg	catgatttag	180
cggctccggt	cattgctggc	attcttgcca	gtatgatcgt	gaactggctg	aacaagcgga	240
agtaacgtgt	catgcggggc	tcaggctgcc	gtaatggcaa	tttgcgccc	gaccaggccg	300
caggggggaa	actctgcggc	ctttttcggt	cttactgcgg	gtaaggcacc	cagtcgccgc	360
cgttcaggcg	aacgtacggg	ttatcctggg	attgaataac	tactgcattt	gagttctcgg	420
agaccggtgc	tgtttggtgc	aaccactggg	tgagtttttt	ccagtcaaca	ttgtcttcgg	480
tgaaaatctt	gccatcgaga	acgcgaacca	ccagatcgga	gatagccagg	aagctgctcg	540
gttggttcgat	gacaatcggt	gccccctgat	gcgggtgcctt	catgccgaag	aatttcaccc	600
caacggggac	gtcgggtgata	gacgggctag				630

<210> 464

<211> 391

<212> DNA

<213> Escherichia coli

<400> 464

ctcaggctgc	tgattgtttt	tttgtgcaat	ggcgcggtat	tagcgtcggt	gctgtcgatg	60
gagagaatca	taaacgtggg	gaatgatgat	tgtagcaag	gaaaactgtc	aaaaatcttc	120
aaaaaatttg	agggataagg	ccggaatggc	tccggccaga	gggaagttaa	ccgcgaagct	180
gttgctgctt	gagggctggt	ttaaccagac	gccaggcgct	ccatacgcca	aaaccgcgtc	240
tggcccagcg	gaccagcata	ttaggatggc	gaatcgcca	gatcgccatc	acgctactgc	300
caaccagcgc	ccaggagcgc	agacttagca	gcataattcca	gcgacgatcg	taagcgctg	360
ttgtctccag	ccattcacga	cgactggcgg	a			391

<210> 465

<211> 625

<212> DNA

<213> Escherichia coli

<400> 465

aacacaccac	accataaacg	gaggcaaata	atgctgggta	atatgaatgt	tttaatggcc	60
gtactgggaa	taattttatt	ttctggtttt	ctggccgcgt	atttcagcca	caaattgggt	120
gactaatgaa	cggagataat	ccctcaccta	accggcccct	tggtacagtt	gtgtacaagg	180
ggcctgattt	ttatgacggc	gaaaaaaaaa	cgccagtaaa	ccggcggtga	atgcttgcat	240
ggatagattt	gtgttttgct	tttacgctaa	caggcatttt	cctgcactga	taacgaatcg	300
ttgacacagt	agcatcagtt	ttctcaatga	atgttaaacg	gagcttaaac	tcggttaatc	360
acattttggt	cgtcaataaa	catgcagcga	tttcttcggg	tttgcttacc	ctcatacatt	420
gcccggctcg	ctcttccaat	gaccacatcc	agaggctctt	caggaaatgc	gcgactcaca	480
cctgctgtca	cggtaatggt	gatatgccct	tcagaatgtg	tgatggcatg	gttatcgact	540
aactggcaaa	ttctgacacc	tgacgacat	gcttcttcat	cattagccgc	tttgacaata	600
atgataaatt	cttcgcccc	gtagc				625

<210> 466

<211> 623

<212> DNA

<213> Escherichia coli

<400> 466

tgcttttgaa	tatgtgctcg	caatcttgag	aaggaaatgg	cgaccacgaa	agaaaaggca	60
aaaacgataa	tctgaaagag	ccaaggtatt	tcagtataag	cattgaatgc	gacagttaac	120
tctttcggta	tcagccagag	agtgcagcca	aaaatgataa	tcgtatacat	aagtccttcg	180
agtggctcgt	tagcaaaaag	tttcaacaat	ggagtaaata	catccaacat	atcaataact	240
ctcaactgta	aggggtattga	aatgttaaca	caagctctcg	ctgtaggggg	atagccgaga	300
ccaccgaagc	ccggagggtg	tgaataaaaa	ccgggcacaa	cacgaaggcg	catttccgat	360
atccataaag	agtcgggtctt	gtctgttaaa	tttaaattgg	gggagtgcgc	ctccggttgt	420
aaataacgac	attgctgtgt	gtagtctctg	cggcacatcag	ttttttcttg	aagttcggct	480
gatgtccgcc	cttttttaag	tgaattttgt	gatgcgggtga	atgcggctaa	gcgcacgtgg	540
cacagttaaa	agtcattgta	gtccttattg	gtttgggtgg	gaaagccgac	tgtaattggt	600
aactgggtgc	agtcacctgg	agg				623

<210> 467

<211> 234

<212> DNA

<213> Escherichia coli

<400> 467

tgtttactta	caagagattc	atctttgtat	aaataaagat	aagtaattac	gcataaaaca	60
acaatgatta	taatagcaaa	aataaatatt	atcatctttg	atagattact	tgagatagcc	120
agcatcttgt	aaagccttta	tcgttttttt	atgctctgga	ttaatataat	cactacatct	180
atctgagcaa	tctgttgttg	atggacatgt	caacccatgg	tcatttacag	ccaa	234

<210> 468

<211> 529

<212> DNA

<213> Escherichia coli

<400> 468

attagctatt	tgggctaaaa	tagagactac	atgtcttcgg	tccatctcac	ttaaggagtg	60
tagttccggt	gtaagttttt	ccatagcttg	cactgctaaa	tttcgaacaa	ggaattttct	120
gctggtaatc	tctaaaaaga	tggcatgggt	tacaatgatt	tttgtttcct	tttgattatt	180
atgaacaact	gtccatgatt	tcgtttaaga	atgaagagaa	atcactaaac	gaactgaata	240
tattttctgt	gccaatatta	tctctaattt	caaaaaagtt	acttttaatg	tcggtaatga	300
ctccaactta	ttgatagtgt	tttatgttca	gataatgcc	gatgactttg	tcatgcagct	360
ccaccgattt	tgagaacgac	agcgacttcc	gtcccagccg	tgccaggtgc	tgccctcagat	420
tcagggttatg	ccgctcaatt	cgctgcgtat	atcgcttttc	cttatcagtt	cgttgatgtc	480
agtggttttg	accacgaggg	agcttcacgc	gagttattga	aaaccctga		529

<210> 469

<211> 261

<212> DNA

<213> Escherichia coli

<400> 469

caaagaacct	tcaacatgaa	aaatatccat	ttgtttgcaa	aaaaagatta	ttaggaagga	60
aattaatgca	attatcgaaa	attcaaaaaa	tatccaaaaa	tagtatactt	tattccagaa	120
gagttcaata	taatgtttgt	cttcaatttt	tcttacttca	gggtaatata	gattgctcat	180
tacattgtga	gcttcatctt	tatttaattt	tctgttgact	ccagctctcc	gtgataacgg	240
ttttataatt	agatgcttat	c				261

<210> 470

<211> 98

<212> DNA

<213> Escherichia coli

<400> 470

agatgattgc	cgggaaacttg	ttagcggcac	gcaggcggcg	gctcgcaccc	ttaccctgct	60
ctttacgtac	ttctgcgttg	atagtaaaca	tttctttc			98

<210> 471

<211> 259

<212> DNA

<213> Escherichia coli

<400> 471

agcgcgaacg	aagtcgatgt	gctgcagctt	cggtttgtac	gggtgacgct	gtacgtcctg	60
agctttaact	ttgatttctt	taccgtcaac	aacgatggtc	agaacttcgc	tgtagaattc	120
agctttagct	tgcatgttca	tgactttgtc	gtgatccagc	tcgatagcca	gcggcgcttc	180
tttgccaccg	tagatgattg	ccgggaactt	gtagcggca	cgcaggcggc	ggctcgcacc	240
cttaccctgc	tctttacgt					259

<210> 472

<211> 94

<212> DNA

<213> Escherichia coli

<400> 472

aaaaacggcg	taaagaaagg	atgcaaacat	gttaataaaa	actcaaattg	atcccacgta	60
tatattacgc	cgcaaaatcc	ttacaataaa	cagg			94

<210> 473

<211> 174

<212> DNA

<213> Escherichia coli

<400> 473

ttaattatta	aaatagtgtg	acgcgattat	gtggttatgg	gggtaaacat	taaataaacc	60
agcggggagg	ggaggtaaag	tgaaaaaata	aaaagcggat	aatcttaata	agcaggccgg	120

acagcatcgc catccggcac tgatacgagg tttatttcag ctcatcaacc atcg 174

<210> 474

<211> 138

<212> DNA

<213> Escherichia coli

<400> 474

ctgtaaaaaac gtcaaaaaaga gtgttttatc aacagaagaa tggaggtctg acagatagta 60
gtaatgcaaa aaaatggaga cttaagttga atgaacggga gtaaagcgaa aagactatag 120
agtgaaggag aaattccc 138

<210> 475

<211> 191

<212> DNA

<213> Escherichia coli

<400> 475

tttgttggct taatattcta ttgttatctt tatttataga tgtttatatt gcatgaggtg 60
gtttttggag agaagaatga ggaagatgcg tcgagccaca gaaacgtag ctttacatat 120
agcggaggtg atgtgaaatt aatttacaat agaaataatt tacatatcaa acagttagat 180
gctttttgtc g 191

<210> 476

<211> 245

<212> DNA

<213> Escherichia coli

<400> 476

cggccatttta tacaggaaaa gcctatgtca gaacgtaaaa actcaaaatc acgccgtaat 60
tatctcgtaa aatgttcctg cccaaactgc acccaagagt cagaacacag tttttcaaga 120
gtacaaaaag gtgccctttt gatctgccct cattgcaaca aagtattcca gacaaatctt 180
aaagctgtag cctgattgat tttattagta acaagtattt tttatatatt aataatatat 240
ttaaa 245

<210> 477

<211> 319

<212> DNA

<213> Escherichia coli

<400> 477

aaattttcag gtacctgtgc accatacttt tttttctgag cattaatgat attttgagct 60
tcttgaggat ctttaactcc ccacatttgg tggaagat tcatattaaa aggaaggttg 120
aataatttgt ctttataaat cgccagtgga gaattagtaa aacgattaaa ttctactaaa 180
tcattaacgt aatcccatat atatttatca ttggtatgaa aaatatgtgc accatattta 240
tgaatctgga taccctcaca gtcctctgtg tacgcatttc caccgatatg atttcttttc 300
tcaatcacta aaacttttt 319

<210> 478

<211> 149

<212> DNA

<213> Escherichia coli

<400> 478

gcagtgatcg aagcgatgac gaagtgtatg gaaaaatcag aaaaactcag caaatcctga 60
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- (71) Applicant: ELITRA PHARMACEUTICALS, INC.
[US/US]; Suite A, 3510 Dunhill Street, San Diego, CA 92121 (US).
- (72) Inventors: ZYSKIND, Judith; 8514 La Jolla Scenic Drive, La Jolla, CA 92047 (US). OHLSEN, Kari, L.; 3560 Vista De La Orilla, San Diego, CA 92117 (US). TRAWICK, John, D.; 7210 Baldrich Street, La Mesa, CA 91942 (US). FORSYTH, R., Allyn; 1135 Beryl Street, San Diego, CA 92109 (US). FROELICH, Jamie, M.; 5057 35th Street, San Diego, CA 92116 (US). CARR, Grant, J.; 2210 Sunrise Glen, Escondido, CA 92029 (US). YAMAMOTO, Robert, T.; 3725 Norte Dame Avenue, San Diego, CA 92131 (US). XU, H., Howard; 11142 Ivy Hill Drive, San Diego, CA 92131 (US).
- (74) Agent: REISMAN, Joseph, M.; Knobbe, Martens, Olson & Bear, LLP, 16th Floor, 620 Newport Center Drive, Newport Beach, CA 92660 (US).
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN *ESCHERICHIA COLI*

(57) Abstract: The sequences of nucleic acids encoding proteins required for *E. coli* proliferation are disclosed. The nucleic acids can be used to express proteins or portions thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous genes that are required for proliferation in microorganisms other than *E. coli*. The nucleic acids can also be used to design expression vectors and secretion vectors. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms as well as to screen for antimicrobial agents.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/02200

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/31 C12N15/11 C12N15/10 C07K14/245

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, STRAND, BIOSIS, BIOTECHNOLOGY ABS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	POST L E ET AL: "NUCLEOTIDE SEQUENCE OF THE RIBOSOMAL PROTEIN GENE CLUSTER ADJACENT TO THE GENE FOR RNA POLYMERASE SUBUNIT BETA IN ESCHERICHIA COLI" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA,US,NEW YORK, NY, vol. 76, no. 4, 1 April 1979 (1979-04-01), pages 1697-1701, XP000574791 abstract	1
A	WO 99 02673 A (DUGOURD DOMINIQUE ET AL.) 21 January 1999 (1999-01-21) page 7, line 25 -page 9, line 30 examples 2-6 -/--	1



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

13.11.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

De Kok, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/02200

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 21366 A (QBI ENTERPRISES LTD) 22 May 1998 (1998-05-22) page 8, line 9 - line 13 page 21, line 30 -page 25, line 2 page 26, line 11 -page 27, line 35 ---	
X	BLATTNER F R ET AL: "THE COMPLETE GENOME SEQUENCE OF ESCHERICHIA COLI K-12" SCIENCE., vol. 277, 5 September 1997 (1997-09-05), pages 1453-1462, XP002923023 LANCASTER, PA., US ISSN: 0036-8075 the whole document, especially figure 3 ---	8,9
X	VAN HEESWIJK W.C. ET AL.: "The genes of the glutamine synthetase adenylation cascade are not regulated by nitrogen in Escherichia coli" MOLECULAR MICROBIOLOGY, vol. 9, 1993, pages 443-457, XP000926027 OXFORD GB nt4271-4371 of glnE sequence 100% identical with ntl-100 of seq.id.165 abstract ---	9
A	LEE N.G. ET AL.: "Molecular cloning and characterization of the nontypable Haemophilus influenzae-2019 rfaE gene required for lipopolysaccharide biosynthesis" INFECTION AND IMMUNITY., vol. 63, no. 3, 1995, pages 818-824, XP000953326 WASHINGTON., US ISSN: 0019-9567 the whole document ---	8
A	AUSTIN A.E. ET AL.: "Genetic analysis of lipopolysaccharide core biosynthesis by Escherichia coli k12 insertion mutagenesis of the RFA locus" JOURNAL OF BACTERIOLOGY, vol. 172, 1990, pages 5312-5325, XP000926028 WASHINGTON US the whole document --- -/--	8

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/02200

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>VALVANO M.A. ET AL.: "The rfaE gene from Escherichia coli encodes a bifunctional protein involved in biosynthesis of the lipopolysaccharide core precursor ADP-L-glycero-D-manno-heptose." JOURNAL OF BACTERIOLOGY, vol. 182, January 2000 (2000-01), pages 488-497, XP000926030 WASHINGTON US the whole document -----</p>	8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/02200

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 11 13 34-45 47 48 50 51 53 55 57-63 65 67-93 95-105 107-110
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-10, 12, 14-33, 46, 49, 52, 54, 56, 64, 66, 94 and 106, all partially

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11 13 34-45 47 48 50 51 53 55 57-63 65 67-93 95-105 107-110

In view of the large number and also the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protection is sought, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely the nucleic acid sequences as identified in claims 1 and 8 respectively, sequences related to said sequences as well as their use. This corresponds to the subject-matter of claims 1-10, 12, 14-33, 46, 49, 52, 54, 56, 64, 66, 94 and 106.

It should be noted that since claim 46 has been searched, the subject-matter of claims 35-45 has been searched restricted to the gene products of claim 46, i.e. for those gene products for which (additional) search fees have been paid

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-7, 12, 49, 52, 56, 66, all partially

Invention 1:

A purified or isolated nucleic acid sequence consisting of SEQ.ID. No.: 405, a vector comprising said sequence, a host comprising said vector, the use of said sequence for inhibiting cellular proliferation, a composition comprising said sequence, the use of said sequence for inhibiting the expression of a gene and the use of said nucleic acid sequence for identifying bacterial strains.

2. Claims: 1-7, 12, 49, 52, 56, 66, all partially

Inventions 2 to 81:

Idem as invention 1, but for SEQ.ID.No's 406-485 respectively

3. Claims: Claims 8-10,12,14-33,46,54,64,66,94 and 106, all partially:

Invention 82:

A purified or isolated nucleic acid consisting of SEQ.ID.No.: 82, a vector comprising said nucleic acid sequence, a host comprising said vector, a polypeptide encoded by said nucleic acid sequence and having the sequence of SEQ.ID.No.: 243, an antibody binding said polypeptide, a method for producing said polypeptide, a method for identifying compounds influencing the activity of said polypeptide, a method for identifying compounds influencing the level of said polypeptide, a method for inhibiting the expression of said nucleic acid, the use of said nucleic acid sequence for identifying bacterial strains and the use of said nucleic acid sequence for identifying proliferation inhibitors.

4. Claims: Claims 8-10,12,14-33,46,54,64,66,94 and 106, all partially:

Inventions 83 to 242:

Idem as invention 82, but for SEQ.ID.No's 83-88, 90-242 (and their corresponding polypeptide sequences, see Table II) respectively.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 00/02200

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9902673 A	21-01-1999	AU 8327798 A EP 1025219 A	08-02-1999 09-08-2000
WO 9821366 A	22-05-1998	AU 5442198 A EP 0960212 A	03-06-1998 01-12-1999

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